



# SURGERY

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# SURGERY

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## Original Communications

### ABDOMINAL SURGERY IN THE EVACUATION HOSPITAL

#### EXPERIENCE WITH 335 ABDOMINAL INJURIES IN THE CAMPAIGN IN NORTHERN EUROPE

CAPTAIN ROBERT W. PEARSON, CAPTAIN JOHN H. TUNY, AND LIEUTENANT COLONEL CHARLES STUART WELCH, MEDICAL CORPS, ARMY OF THE UNITED STATES

**D**URING a six-month period of intermittent operation in the course of the campaign in Northern Europe, 335 patients with abdominal injury were treated in an evacuation hospital. These wounded represented 3.6 per cent of the total battle casualties received during the same period. For the most part the patients were American soldiers and prisoners of war in the young adult class, although a number of civilians were treated, among whom extremes of age were encountered.

The hospital functioned under tentage at all but one station. The operating tents, which provided ten tables, were connected with the shock and pre-operative wards and with the x-ray department. These patients were operated upon by permanent and attached members of the surgical service, under the direction of one of us (C. S. W.).

It has been well established that the results obtained in abdominal surgery in World War II are far better than in previous wars. Although the morbidity rate has increased, the operative mortality rate has been markedly reduced. This has been brought about chiefly by more efficient and rapid transportation to the hospital, better supportive treatment with blood, plasma, and oxygen, improved surgical methods, including anesthesia; and therapy with sulfadiazine and penicillin.

The operative mortality and results which we shall present are based upon the immediate recovery from surgery, representing usually a ten-day post-operative period, up until the time that the patient was considered to be safely dischargeable. Thus, they are the results of the surgeon working in the field, in a specialized echelon of surgery.

We are aware that additional morbidity and mortality will occur from secondary operations and from late postoperative complications. These statis-



ties, however, are not known to us at this time, but judging from the condition of our patients on evacuation, we would expect the additional mortality to be small.

#### CLINICAL FINDINGS ON ADMISSION

*Classification.*—From the clinical standpoint we found that wounds involving the abdomen fell into one of three groups, depending upon the location of the wound of entrance. These were (1) the classical penetrating or perforating wounds which enter the abdomen from the front or back, which we have designated as the *abdominal* group; (2) wounds of the buttocks, perineum, and lateral aspect of the hip below the level of the greater trochanter of the femur, associated with suspected involvement of the intestinal tract or bladder, which we have called the *pelvicobdominal* group, and (3) combined injuries of the thorax and abdomen, which we have designated as the *thoracobdominal* group.

The *abdominal* group was the largest (169 cases).

The *pelvicobdominal* group, made up of eighty-three cases, carried the lowest mortality rate, and comprised injuries not commonly seen in civil practice. They resulted largely from the fact that soldiers are frequently hit when crouching or lying prone, and sometimes are wounded by mine explosions. Commonly the injuries were limited to the extraperitoneal rectum and bladder, and consequently presented special problems in diagnosis and treatment.

The *thoracobdominal* group also included eighty-three cases and carried a somewhat higher mortality rate than the other groups. These cases presented the most complicated problems, since both body cavities were involved, and at times major operative interference in both the chest and abdomen was required.

The proportionate number of cases in the three groups (2:1:1, respectively) reported in this series probably represents their actual incidence in this campaign, since in the evacuation hospital, functioning as it did at varying distances from the front, all of the more seriously wounded were treated with no selection of cases. Furthermore, during this six-month period, casualties were received which were the result of both mobile and static warfare.

The statistics which follow apply only to the 303 patients operated upon. The thirty-two nonoperative cases are discussed in the section entitled Operability, but they have been omitted in compiling the general statistical data, since usually the exact nature of the injuries could not be determined. The condition of the patients precluded thorough examination during the short time they lived and no autopsies were performed. The omission of these cases should in no way be interpreted as an attempt to minimize their importance, however.

*Location of Wounds.*—In the *abdominal* group there was a fairly uniform distribution of wounds in each of the four quadrants of the abdomen and in the flanks and lumbar regions. In the *pelvicobdominal* group, wounds of the buttocks greatly predominated over those of the perineum and thigh. In the *thoracobdominal* group, right-sided wounds outnumbered left-sided in the

ratio of four to three, presumably because left-sided wounds are more likely to be fatal on the battlefield. In addition, the wounds were more commonly lateral or posterior, due to the greater exposure of these regions in combat attitudes, and to the fact that anterior wounds are also more often quickly fatal. The missile traversed the pleural cavity before entering the abdomen four times as often as primary penetration of the abdomen with secondary involvement of the thorax. In nearly all of the thoracoabdominal cases, the wound of entrance was between the transverse plane of the nipples and that of the umbilicus. The size of the external wound was not a reliable indication of the degree of internal damage.

*Causative Missiles*.—Analysis of the type of causative agent in the patients operated upon indicated that 76 per cent of the wounds were due to shell fragments (the term being used to include fragments of artillery shells, aerial bombs, grenades, mines, and booby traps), 22 per cent to bullet wounds, and 2 per cent to blunt trauma, mostly the result of vehicle accidents.

Shell fragment wounds were most common in the thoracoabdominal group, where they were six times as frequent as bullet wounds. They were only 2.5 times as common in the pelvicabdominal group.

The missile wounds were penetrating in type in 79 per cent, perforating in 19 per cent, and both penetrating and perforating in 2 per cent. Bullets, of course, had a greater perforating tendency (three perforating to two penetrating wounds). This was most marked in the abdominal group, where five out of six bullets perforated whereas only one out of eight shell fragments perforated the abdomen. On the other hand, only about one-third of the gunshot wounds and less than one-twentieth of shell fragment wounds in the pelvicabdominal group were perforating in type, due undoubtedly to the greater warding effect afforded by the bony pelvis and soft tissues.

*Condition on Admission*.—The patient's condition on admission is the result of a number of factors, most important of which is shock due to trauma and hemorrhage. Other important factors include the multiplicity and severity of associated injuries, respiratory and circulatory disturbances due to concomitant wounds of the thorax, evisceration, and exhaustion, anxiety, and exposure. By evaluation of these factors, the patient's condition was described by one of the following terms: (1) good, (2) fairly good, (3) fair, and (4) poor. In most cases this grouping corresponded to the degree of shock present, that is none, slight, moderate, and severe.

The percentage of patients in poor condition on admission varied greatly from one station to another, depending upon the tactical situation, the highest being 32 per cent and the lowest 6 per cent. The operative mortality rates for these four groups rose from 17 per cent for patients admitted in good condition to 50 per cent for those admitted in poor condition.

An analysis of operative cases with perforated viscera in the abdominal group is given in Table I. It will be noted that the average interval between wounding and admission was only 1.7 hours longer for patients in poor condition (where the mortality rate was 48 per cent) than that for those in good condition (where the rate was 0). Part of this increase in time lapse was accounted

TABLE 1. CONDITION ON ADMISSION IN 115 PATIENTS OPERATED UPON WITH PERFORATED VISCERA IN THE ABDOMINAL GROUP

CONDITION ON ADMISSION	AVERAGE HOURS BETWEEN WOUNDING AND ADMISSION	MODERATE OR SEVERE ASSOCIATED INJURY (PER CENT)	OPERATIVE MOR- TALITY RATE (PER CENT)
Good	7.5	33	0
Fairly good	6.8	38	14
Fair	7.9	41	25
Poor	9.2	52	48

for by the necessity of delay in forward echelons for the treatment of severe shock. It is true that associated injuries were somewhat more frequent in patients in poor condition, but this increase also by no means paralleled the progressive increase in the operative mortality rate.

The estimation of the patient's general condition, therefore, offers the best single preoperative guide to prognosis.

*Preoperative Complications*—The most frequent preoperative complications were those peculiar to thoracoabdominal injuries. These included open pneumothorax (25 cases), moderate to severe hemothorax (24 cases), hemothysis (18 cases), moderate or severe intrapulmonary bleeding (11 cases), diaphragmatic herniation (7 cases), and atelectasis (2 cases).

Evisceration was the most important complication in the abdominal group (12 cases). In addition, four cases were observed in the thoracoabdominal group, and two in the pelvicoabdominal group. Evisceration of the omentum only was present in seven of the eighteen cases, and then was significant primarily as an indication of abdominal penetration.

Certain other preoperative complications were also more important from the diagnostic standpoint than per se. Some of these were hematemesis (2 cases), drainage from the wound of urine (25 cases), feces (5 cases), gastric content or bile (2 cases), and hemothorax or hemoperitoneum fluid.

Hemorrhage from the wall of the chest or abdomen was of importance in relatively few cases. Morphism was well marked in one case. Preoperative transfusion reactions were severe in three cases.

Preoperative subacute or chronic bronchitis was not infrequent among soldiers, many of whom were heavy smokers, and this fact undoubtedly had a bearing on the incidence of postoperative atelectasis and bronchopneumonia.

*Associated Injuries*—Extra-abdominal injuries associated with abdominal wounds are an important cause of morbidity and mortality. Exclusive of minor wounds, they were present in 55 per cent of all patients operated upon in this series, and were considered to be the chief cause of death in six cases, and the secondary cause in at least twelve cases.

Associated injuries may be described as related or unrelated to the abdominal lesions. Related injuries are caused by the same missile which produced the abdominal injury, for example, fractures of the spine or pelvis. Unrelated injuries are caused by a different missile, nearly always another shell fragment.

When small flesh wounds are excluded, the associated injuries can be divided into three groups: moderate, moderately severe (for example, fractures

of the long bones, skull, pelvis, or spine), and severe (for example, transection of the spinal cord, severe intracranial injuries, and fractures of an extremity associated with vascular damage). The injuries in the patients operated upon were classified as moderate in 24 per cent, moderately severe in 20 per cent, and severe in 11 per cent. The combination of associated injuries in patients with abdominal wounds has little counterpart in civil practice, where the abdominal injury is usually the only one. Some examples of the most serious associated injuries are given here.

*Spinal cord injuries:* There were eight patients (three deaths) with involvement of one or two vertebrae from the tenth dorsal to second lumbar inclusive, of whom five had complete transection. Laminectomy was performed in only one patient.

*Intracranial injuries:* Three cases with penetrating wounds of the brain were encountered, and in each case craniotomy was deferred until the day following abdominal operation. The only death occurred five hours after an extensive bilateral frontal craniotomy in a patient who had withstood a right hemicolectomy the preceding day.

*Compound fractures of the femur:* The seriousness of this injury associated with abdominal trauma is well recognized. Gordon-Taylor<sup>1</sup> has described this combination as "a burden hardly to be borne by suffering humanity." In this series four of nine such patients died.

*Amputations:* Six patients in this series had major amputations of an extremity, of whom two died. In all but one case, in which completion of a partial traumatic amputation was carried out, the amputation was deferred for three to ten days after the abdominal operation.

*Intrathoracic injuries:* Seven patients, not included in the thoracoabdominal group, had some intrathoracic injury associated with sufficient abdominal signs to induce the surgeon to perform a laparotomy. In one case perforated abdominal viscera were found, and two patients had evidence of intra-abdominal blast injury. In the other three cases the pulmonary injury was due to blast, but none of blast have not been placed in the thoracoabdominal group since the causation and management are different from those of thoracoabdominal wounds. In the other four cases there were penetrating wounds of the pleural cavity but laparotomy was negative, and so by definition these cases were also excluded.

*Principles of Treatment of Associated Injuries*—The abdominal or thoracoabdominal operation should be performed first, since it is a lifesaving procedure and cannot be postponed, nor abandoned once begun. In addition, it often improves the condition of the patient, in contrast to operations upon the extremities which tend to increase shock. Furthermore, operations on the extremities are not compelling (except in the case of partial traumatic amputation, major vessel injury, or gas bacillus infection), and one is not committed to finish the procedure if the patient's condition deteriorates. Sulfadiazine and penicillin therapy have so greatly lessened the risk of sepsis that deferment of such operations for twenty-four to forty-eight hours when necessary is justifiable.

In the case of compound fractures with emergency methods of traction, skin traction should be substituted until the deferred operation can be per-

formed. In very poor risks where it is anticipated that the patient cannot be returned to surgery for several days, the best temporary expedient is the enlargement of deep wounds to provide adequate drainage. In fact, for clean wounds of the soft tissues this treatment may suffice.

In most cases operation on the abdomen and extremities should not be carried out simultaneously, since the increased operative shock is not compensated for by the time saved. After the vital operation has been completed the decision to perform or defer the treatment of the associated injuries can be made.

#### DIAGNOSIS

The diagnosis of intra abdominal injury was easily made in the majority of cases on the basis of the location of the wounds, especially if they were perforating in type, and on the presence of unmistakable signs and complications.

Anteroposterior and lateral roentgenograms of the abdomen were made almost routinely, and were of the greatest value in establishing the presence of abdominal penetration. In a few cases roentgenograms were not made, either because the wounds were perforating or because of the desperate condition of the patient and the obvious nature of the injuries.

The difficulties encountered in the diagnosis of perforated viscera are attested to by the number of laparotomies at which none was found (55, or 19 per cent of the major operation cases). Only twenty three cases (8 per cent) actually represented negative explorations, however, since the others had some intra or retroperitoneal damage or foreign body.

Although attempts were made to keep the number of negative abdominal explorations at a minimum, it was thought best because of the low morbidity and mortality of the operative procedure to carry out exploration in any doubtful cases, for the following reasons:

(1) The signs of visceral perforation, especially if due to small fragments, may be minimal. Explorations were done in several such cases, and although the surgeon felt that they would prove to be negative, intestinal perforations were found.

(2) The tendency to explain physical signs as being due to retroperitoneal hematoma alone must be guarded against, for a retroperitoneal intestinal perforation may also be present and may easily prove fatal, even though the resulting infection is drained later.

(3) The path of the missile from its entrance to exit or point of lodgment is not always straight, especially in the case of shell fragments.

(4) Even though the missile has not entered the peritoneal cavity, it may have damaged retroperitoneal structures, such as the kidney, ureter, pancreas, or major blood vessels.

(5) Indriven bone fragments, such as those from the ilium, may have perforated a viscus and yet not be visible in the roentgenograms.

(6) Missiles with high velocity may cause severe damage at distances of several inches from the actual tract by reason of the concussion wave imparted.

to the tissues.<sup>2</sup> For example, in our series the kidney was contused or lacerated in three patients without having been struck by the missile.

(7) Finally, it is frequently impossible to say definitely from the roentgenograms whether or not a foreign body is intraperitoneal, especially when it has entered the posterior abdominal wall.

Special aspects of diagnosis in the three groups of cases are discussed here.

*Abdominal Group*—While the classical signs of peritoneal irritation were usually present in cases with perforation of the gastrointestinal tract, the signs were sometimes equivocal when there was little or no bleeding or leakage of gastrointestinal content. On the other hand, these signs may be present when a foreign body or bone fragment is lodged in contact with the peritoneum, or when abdominal blast injury has occurred.

The question of penetration of the abdominal cavity may sometimes be decided by exploration of the wound tract. However, the latter is often lost in the deep muscular layers of the flank and lumbar regions, and one may still be unable to determine whether penetration has occurred.

*Pelvicabdominal Group*—The first principle in the management of these cases is to assume that all wounds of the buttocks and perineum involve the intestinal or genitourinary tracts until proved otherwise. This means that all these patients must have roentgenograms of the abdomen and pelvis, unless the position of a wound of exit makes it obvious that no pelvic structures could have been injured.

It is especially important during the physical examination to search carefully for wounds of the buttocks and perineum, since they may be easily overlooked (especially in patients with a Thomas splint), and since signs of penetration of the abdomen are often absent.

Blood found on rectal examination is diagnostic of rectal perforation except in rare cases of abdominal blast injury. Unless the perforation is felt, sigmoidoscopy should be performed in all cases, even if there is no blood on the examining finger, since the presence of extraperitoneal perforation cannot be determined at laparotomy. All patients should be catheterized before operation whether they can void or not, and whether or not hematuria is present.

*Thoracoabdominal Group*—The possibility of concomitant injury to the abdomen in patients with a thoracic wound should always be borne in mind, particularly if the wound of entrance is at or below the plane of the nipples. The physical signs of abdominal involvement in such cases are unreliable, since abdominal distention, rigidity, and tenderness frequently accompany wounds of the lower thorax, especially if they are associated with rib fractures. The crux of the diagnosis is the roentgenographic location of all missiles with a reconstruction of their course, and therefore in all wounds of the lower thorax or upper abdomen, anteroposterior and lateral roentgenograms of both chest and abdomen must be obtained.

#### MORTALITY

Of the 335 patients with abdominal injury, 77 died, a total mortality rate of 23.0 per cent. Five do not require operation and were treated expectantly.

Three hundred and three of the 330 remaining patients were operated upon, an operability rate of 91.8 per cent. The rate was lowest in the thoracoabdominal group (87.5 per cent) and highest in the pelvicabdominal group (96.4 per cent).

Of the 32 patients not operated upon, 27 died, two-thirds of them within twelve hours of admission, usually of shock which did not respond to supportive treatment. Six of these patients had severe associated injuries which of themselves contributed to the fatal outcome.

Of the twenty-seven nonoperative deaths, one occurred on the eighth day due to peritonitis from an unrecognized perforation of the sigmoid in a patient with a compound fracture of the femur. Another patient with a transection of the spinal cord, hematuria, and severe retroperitoneal hematoma, died on the seventh day after admission. The remaining twenty-five patients represent that important group in which a decision against operation was made on the basis of their extremely poor condition and inability to withstand operative interference in spite of vigorous supportive therapy.

Except in cases where operation would certainly prove fatal, every attempt was made to operate upon desperately wounded patients if it was thought that further shock therapy could do no more to improve their condition. The arrest of hemorrhage at operation may offer them their only chance of survival. Eleven patients died on the operating table during surgery or immediately afterward in the course of such procedures, but several others with an almost equally bad outlook survived. It is almost a truism that the surgeon should be concerned with the over all mortality rate, rather than with the operative mortality rate alone.

In five patients no operation was thought to be indicated. One woman, a civilian, wounded four days before admission had an intraperitoneal foreign body and minimal signs of peritoneal irritation. Another patient with a laceration of the kidney and retroperitoneal hematoma due to blunt injury was also cared for expectantly. In the thoracoabdominal group, there were three patients with shell fragment wounds of the right lung and liver likewise treated conservatively.

#### PREOPERATIVE TREATMENT

Patients with signs of shock were treated in a shock ward adjacent to the operating room. Oxygen therapy and infusions of blood and plasma were begun at once when indicated.

The refrigerated type O blood used was either whole blood or blood mixed with an equal volume of Aksever's solution. The former was preferred for patients in poor condition where it was anticipated that 1,500 c.c. of blood or more would be needed. There was a real danger of overloading the vascular system and precipitating pulmonary edema in such cases by the administration of even moderate amounts of blood when it was mixed with fluid. This was especially true in thoracoabdominal cases with much hemothorax or lung damage. Concentrated plasma was used in both prevention and treatment of such pulmonary edema with good results.

The amount of blood given depended upon the estimated blood loss, the patient's response to therapy, and the hematocrit reading. The question of the presence or absence of continuing intra-abdominal bleeding had to be decided quickly on the basis of the clinical findings, rather than upon serial hematocrit studies over a period of time.

Many casualties had received plasma, and a few received blood transfusions as well, at forward medical units. In the hospital, 55 per cent of the patients were given transfusions before or during surgery. The average amount of blood given corresponded with the degree of shock as follows: for patients in good condition, 750 c.c., in fairly good condition, 950 c.c., fair condition, 1,400 c.c., and poor condition, 2,750 c.c. In addition, many of these patients received one to six units of plasma. Dextrose or saline infusions were given to a few patients who were in good condition.

Oxygen therapy by nasal catheter was given an increasingly wide application as its value for patients in shock became more and more appreciated.

Gastric suction was instituted in patients with abdominal distention and in those who showed gastric dilatation in the roentgenograms.

Penicillin therapy was given routinely on admission with a dose of 20,000 units intravenously and 20,000 units intramuscularly. The latter was repeated every four hours, except in pelvic-abdominal cases, where it was given every two hours. Sulfahazine was not administered orally to patients suspected of having penetrating wounds of the abdomen, nor was it our policy to give the drug intravenously before operation.

Aspiration of a hemopneumothorax large enough to cause dyspnea was carried out in seven of the thoracoabdominal cases.

When possible, operation was delayed until the systolic blood pressure had reached a minimum of 100 mm. of mercury and the pulse rate was less than 120 beats per minute. Some patients, however, obviously needed an immediate operation for the arrest of hemorrhage and were operated upon while in shock.

#### TIME LAG

The interval between wounding and admission varied with the proximity of the hospital to the front and with the condition of the patient, for example, whether or not he had been detained in advanced medical installations for shock therapy. This interval averaged 8.4 hours, and was shortest in the thoracoabdominal cases (6.2 hours) and longest in the pelvic-abdominal cases (8.9 hours).

The interval between admission and surgery could be controlled to a large extent by the surgeon, although occasionally the large number of other urgent cases on the operating schedule necessitated delay beyond the optimum time. The average of this "hospital time" for the operative cases was 8.5 hours. It was longest in the thoracoabdominal patients (11.4 hours), in whom perforated hollow viscera were less frequent, and in whom operation could more safely be delayed. It was shortest in the abdominal group (7.3 hours).

The total time lag between wounding and surgery therefore averaged 16.1 hours, which was about equally divided between transportation to the hospital



and time spent in the hospital. (This is only one hour shorter than that reported by Rohlf and Snyder in the Tunisian Campaign.<sup>3</sup>) The averages for the three groups were: abdominal, 15.7 hours, thoracoabdominal, 17.6 hours, pelvioabdominal, 18.6 hours.

We did not follow a policy of designating some definite time lag as an interval after which we would not perform laparotomy; several patients were operated upon over forty-eight hours after being wounded. The decision must be made on the ability of the patient to withstand operation, the nature of the injuries, and the degree of peritonitis present.

In the past, great emphasis has been placed on the importance of shortening the interval between wounding and surgery. It was felt that as little time as possible should be spent in supportive treatment since every hour was important. During World War II, however, the idea gained ground that supportive therapy must be fully adequate, and especially that lost blood must be replaced by blood. Two or three additional hours spent in allowing the patient to stabilize more than compensate for the added risk of peritonitis, which with chemotherapy is no longer as great a hazard as formerly.

The operative mortality rate does not rise significantly for patients wounded six, twelve, and eighteen hours. In our series the operative mortality rates for these intervals were: six hours, 13 per cent, twelve hours, 13 per cent; eighteen hours, 16 per cent. Furthermore, Ogilvie<sup>4</sup> reported a higher rate for those wounded under twelve hours than for those wounded over twelve hours. This might give the surgeon the impression that the time lag had lost most of its time-honored importance. However, improved shock therapy and prompt evacuation have permitted many seriously wounded casualties to live to reach the hospital and to be operated upon a few hours after being wounded. These poor risk patients, who in World War I would have died en route, swell the operative mortality rates in the six-hour and twelve-hour groups to approach that of the eighteen-hour group.

#### OPERATIVE MANAGEMENT

Three hundred and three of the 333 patients in this series were operated upon. Data on these cases are presented in Table II.

Injury to one or more viscera was found in 235 of the 290 cases in which major operation was performed. Exploration of the abdominal cavity was negative in twenty-three cases. In thirty-two others, while there was no visceral perforation, there were other intra-abdominal injuries varying in severity from large retroperitoneal hematomas and lacerations of the mesentery to minor serosal tears and organ contusions. In some, a foreign body had entered or traversed the peritoneal cavity without causing any appreciable damage.

Operations classified as minor procedures were carried out in thirteen patients, all of whom had perforated viscera, except one patient in the thoracoabdominal group in whom only the lateral attachment of the diaphragm had been torn. Injury to the liver in six cases, to the kidney in two, and to the spleen in one case was not severe enough to warrant exploration, and wound débridement sufficed. In two other patients, one of whom died drainage of

TABLE II. DATA ON 303 PATIENTS OPERATED UPON

OPERATION	ABDOMINAL			PELVIC ABDOMINAL			THORACO ABDOMINAL			TOTALS		
	NUM RER	DIED	PER CENT DIED	DIED	NUM RER	PER CENT DIED	NUM RER	DIED	PER CENT DIED	NUM RER	DIED	PER CENT DIED
Total of major operations	147	26	17.7	80	11	13.8	63	12	19.0	290	49	16.9
(1) Perforated viscera	109	21	21.1	67	11	16.4	50	11	18.6	235	45	19.1
(2) No perforated viscera, other intra-abdominal injury present	20	1	15.0	8	0	0.0	4	1	25.0	32	1	12.5
(3) Negative laparotomy	18	0	0.0	5	0	0.0	0	0	0.0	23	0	0.0
Total of minor operations	6	1	16.7	0	0	0.0	7	0	0.0	13	1	7.7
(1) Perforated viscera	6	1	16.7	0	0	0.0	0	0	0.0	12	1	8.3
(2) No perforated viscera	0	0	0.0	0	0	0.0	1	0	0.0	1	0	0.0
Total*	153	27	17.6	80	11	13.8	70	12	17.1	303	50	16.5
Total cases with perforated viscera	115	24	20.9	67	11	16.4	61	11	17.0	247	46	14.6
Total cases with no perforated viscera	38	3	7.9	13	0	0.0	9	1	20.0	56	4	7.1

peritoneal abscesses resulting from intestinal perforation was performed. In the thirteenth case, a small perforation of the stomach or jejunum, at first unsuspected, was successfully treated conservatively.

The operative mortality rate in the 303 patients operated upon was 16.5 per cent. The rate for major procedures was 16.9 per cent, and for minor operations 7.7 per cent. Operations on patients with perforated viscera carried a mortality rate of 18.6 per cent. When there was no perforated viscera the rate was 7.1 per cent.

**Abdominal Group**—The incision to be made is largely determined by the site of involvement. In general, upper or lower rectus muscle-splitting incisions were employed. These permitted adequate exploration and exteriorization of injured portions of the right or left colon through separate laterally placed incisions. Exteriorization of the large intestine through the laparotomy incision should be avoided whenever possible to lessen the incidence of wound sepsis and dehiscence. A very useful incision for exploration of the colon and small intestine is a low midline incision, which may be extended above the umbilicus. Transverse incisions for exploration of the upper abdomen and flank incisions were rarely used. When injury to the kidney alone was present the classical lumbar incision was made.

The usual steps in complete exploration of the abdomen were followed. In poor-risk cases, when the path or location of the missile is definitely known, exploration of remote portions of the gastrointestinal tract need not be carried

out. This saves time and reduces operative shock and further dissemination of spillage in the peritoneal cavity.

Drainage of the peritoneal cavity was not employed except in cases with intraperitoneal perforation of the rectum when considerable fecal contamination had occurred, and in most cases with lacerations of the liver. In the majority of cases with perforation of a hollow viscus, a mixture of 5 to 10 Gm. of sulfanilamide powder with penicillin was introduced into the abdomen.

The wound was usually closed in layers with chromic catgut along with silk stay sutures. In a number of cases through-and-through stay sutures alone were employed. Débridement of the wounds of entrance and exit was usually done after closure of the laparotomy incision, and in patients in poor condition without large wounds, it either was performed cursorily or was dispensed with.

Of the 153 patients operated upon in the abdominal group, twenty-seven died, an operative mortality rate of 17.6 per cent. The rate was higher (20.9 per cent) in cases with perforated viscera.

*Pelvicobdominal Group.*—In nearly all cases a low midline incision was made, since it allowed adequate exploration and repair of the intraperitoneal structures usually involved. Even when it seems likely that injury to the rectum or bladder is extraperitoneal, exploration preliminary to sigmoid colostomy is indicated in order to locate and repair any intraperitoneal perforations, such as might occur from bone fragments, and to determine the presence of a retroperitoneal hematoma which in itself was considered to be an indication for colostomy. Furthermore, intraperitoneal perforations of the bladder or injury to the ureters may exist without exhibiting hematuria.

In nearly all cases, sigmoid colostomy through a left McBurney incision is indicated. When the bladder or urethra is injured, suprapubic cystostomy should be performed after closure of the peritoneum.

In patients with wounds of the extraperitoneal rectum, drainage of the presacral space is necessary as well as wound débridement. These should be deferred until the end of the abdominal operation, since if the patient's condition is then poor they may be postponed for twenty-four to forty-eight hours. Turning the patient for these procedures often results in a fall of blood pressure of from 10 to 30 points. To avoid this, presacral drainage may be performed with the patient in lithotomy position if immediate drainage seems necessary, although this position does not give access to the buttock wound.

Presacral drainage was usually effected by an incision lateral to the coccyx, often with coccygectomy, after which Penrose drains were inserted into the presacral space. Drainage of this space through the buttock wound was not considered desirable.

There were eighty patients operated upon in the pelvicobdominal group, of whom eleven died, an operative mortality rate of 13.8 per cent. The rate for patients known or presumed to have a perforated viscus was 16.4 per cent. None of the thirteen patients without visceral perforations died.

*Thoracoabdominal Group.*—The most important aspect of the surgical management of this group is the choice of operation, which depends almost entirely

upon what organs have been injured and to what extent. The decision to operate through the chest, abdomen, or both should be based upon definite indications rather than upon personal choice.

*Thoracotomy with transdiaphragmatic operation:* The decision to perform thoracotomy with transdiaphragmatic operation (thirty cases) should have as its first requisite the presence of sufficient thoracic involvement to warrant thoracotomy, irrespective of the type and extent of abdominal involvement. The usual indications for thoracotomy are (1) large sucking wounds of the chest, (2) severe intrathoracic bleeding, (3) diaphragmatic herniation, (4) mediastinal injury, and (5) the presence of large retained foreign bodies. Fortunately, the three organs most commonly involved in this group (stomach, spleen, and liver) are accessible to transdiaphragmatic exploration and repair, and in fact are more easily operated upon through the chest than by celiotomy.

In nearly all cases, a low posterolateral or anterolateral thoracotomy incision was made to include the wound of entrance, which was excised. Elective incisions were avoided. Resection of fractured ribs was performed in twenty-one cases. Evacuation of the hemothorax, removal of foreign bodies, suture of the lung, and enlargement of the wound of the diaphragm were carried out when necessary. After suture of the diaphragm the chest wall was closed, including the skin, and closed intercostal catheter drainage of the pleural cavity was always provided.

*Thoracotomy with transdiaphragmatic operation combined with laparotomy:* Thoracotomy with transdiaphragmatic operation combined with laparotomy (twelve cases) is indicated when the undersurface of the liver is involved, when perforation of the small or large intestine is present, or when the surgeon is in doubt that the exploration of the abdomen through the diaphragm has been adequate. Fortunately, the intestine was involved in only eight cases in the thoracoabdominal group. Thoracotomy and laparotomy through separate incisions were necessary in only five cases, and then the operation calculated to do the patient the most good (that is, usually thoracotomy) was done first. In seven patients exploration of both body cavities was carried out through the same incision in the flank or upper abdomen.

*Laparotomy alone:* Laparotomy alone, with débridement of the chest wound and thoracostomy or closed intercostal drainage, was carried out in eighteen patients in whom thoracic involvement, while appreciable, did not require thoracotomy.

*Exploration of the kidney and minor procedures:* Exploration of kidney and minor procedures, such as débridement and chest aspiration, were performed in the other ten cases where no indication for either laparotomy or thoracotomy existed.

Twelve of the seventy patients operated upon in the thoracoabdominal group died; an operative mortality rate of 17.1 per cent. Of the forty-two patients subjected to thoracotomy and thoracotomy combined with direct laparotomy, ten died (24 per cent).

TABLE III. ORGAN INVOLVEMENT IN 247 PATIENTS WITH PERFORATED VISCERA

	ABDOMINAL		PELVIC ABDOMINAL		THORACO ABDOMINAL		TOTAL			INCI DENT OF IN VUL MENT IN PA TIENTS
	NUM BER	NUM BER DIED	NUM BER	NUM BER DIED	NUM BER	NUM BER DIED	NUM BER	NUM BER DIED	PER CENT DIED	
Stomach										
Alone	5	1	0	0	5	2	10	3	30	40
With others	3	0	0	0	10	3	13	3	23	53
Total	8	1	0	0	15	5	23	6	26	93
Small intestine										
Alone	31	7	3	0	0	0	34	7	21	137
With others	29	11	7	1	5	1	41	13	32	167
Total	60	18	10	1	5	1	75	20	27	304
Colon										
Alone	17	3	2	1	0	0	19	4	21	77
With others	30	10	3	1	5	1	38	12	32	154
Total	47	13	5	2	5	1	57	16	28	231
Rectum										
Alone	0	0	36	2	0	0	36	2	6	146
Extraperitoneal	0	0	31	2	0	0	31	2	6	
Intraperitoneal	0	0	5	0	0	0	5	0	0	
With others	0	0	7	1	0	0	7	1	14	29
Extraperitoneal	0	0	4	0	0	0	4	0	0	
Intraperitoneal	0	0	3	1	0	0	3	1	33	
Totals	0	0	43	3	0	0	43	3	7	174
Extraperitoneal	0	0	15	2	0	0	15	2	6	
Intraperitoneal	0	0	3	1	0	0	3	1	33	
Bladder										
Alone	0	0	10	4	0	0	10	4	40	47
With others	0	0	6	1	0	0	6	1	17	2
Total	0	0	16	5	0	0	16	5	31	49
Ureter total	2	0	1	0	0	0	3	0	0	12
Liver										
Alone	8	0	0	0	27	3	35	3	9	142
With others	11	1	0	0	12	3	23	4	17	95
Total	19	1	0	0	39	6	58	7	12	237
Spleen										
Alone	3	0	0	0	7	0	10	0	0	4
With others	2	0	0	0	8	3	10	3	30	4
Total	5	0	0	0	15	3	20	3	15	80
Kidney										
Alone	9	1	0	0	5	0	14	1	7	57
With others	6	0	0	0	7	2	13	2	15	52
Total	15	1	0	0	12	2	27	3	11	109
Pancreas total	1	1	0	0	0	0	1	1	100	54
Urethra total	0	0	1	1	0	0	1	1	100	14
Totals	157		76		91		324			

*Management of Injuries to Specific Organs.*—The incidence of injury to the various organs in the 247 patients with perforated viscera, and their respective operative mortality rates, is given in Table III. In this table distinction is made between involvement of each organ alone and involvement with one or more other organs. Seventy per cent of the 247 patients had only one viscus involved and the rest had injury to two or more viscera. With the probably fortuitous exceptions of the stomach and bladder, multiple organ involvement was associated with a higher operative mortality rate. The operative mortality



The operative mortality rate in patients with injuries of the small intestine was 27 per cent. The rate for resection with anastomosis was 33 per cent, as compared with 22 per cent when suture of perforations only was done. However, this greater mortality rate is due rather to the greater severity of the injuries, shock, and preoperative spillage in patients requiring resection than to the procedure of the resection itself.

*Colon:* The intraperitoneal colon and rectum were perforated in sixty-five cases. Injury to the left colon (thirty-five cases) was more frequent than to the right (twenty-one cases) due to its greater length, but the distribution of wounds along the length of the colon was fairly uniform. Five different operative procedures were utilized:

(1) *Exteriorization* of the injured segment (forty-three cases) was the method of choice in nearly all injuries except those of the rectosigmoid and rectum. The bowel was mobilized when necessary and a spur was formed preliminary to exteriorization through a laterally placed incision. This technique was used with an eventual extraperitoneal closure of the colostomy in mind. More recently, formation of a spur has been unnecessary since transperitoneal closure has become the rule.

(2) *Exteriorization resection* was performed in four cases, and we believe it to be the operation of choice for extensively injured segments of the colon. It was done three times for injuries of the right colon requiring hemicolectomy, and once for a severely damaged sigmoid.

(3) *Suture of colon with proximal colostomy* was performed in ten cases. Perforation of the intraperitoneal portion of the rectum and of the rectosigmoid, which is the prime indication for this operation, was present in eight of these cases. Transverse colon colostomy with suture of perforations of the left colon was done twice, but this procedure is not recommended for lesions of any segment of the colon which can be mobilized and exteriorized.

(4) *Closure of perforations of the cecum with catheter cecostomy* was carried out in four patients.

(5) *Suture alone* was done once (for a small perforation of the cecum) but we believe this procedure should be done rarely if ever.

In two patients with perforations both of the cecum and of another portion of the colon, cecostomy and exteriorization of the injured segment were carried out. In the remaining patient there was a perforation of the sigmoid which was not found at laparotomy. This resulted in the formation of a fecal fistula, but the patient lived.

Perforations of the extraperitoneal portions of the ascending or descending colon are best treated as though they were intraperitoneal, that is, by mobilization and exteriorization of the colon, rather than by suture and extraperitoneal drainage.

The operative mortality rate in cases with intraperitoneal perforations of the colon and rectum was 26 per cent.

*Rectum:* The eight injuries to the intraperitoneal rectum have already been discussed in the preceding paragraphs.

The extraperitoneal portion of the rectum was injured in thirty-five other patients. These injuries are listed in Table III under a separate heading because the treatment, complications, and operative mortality rate (6 per cent) differ from those associated with perforation of the rest of the colon. The most important point in the management of perforations of the extraperitoneal rectum is the avoidance of retroperitoneal sepsis by diversion of the fecal stream in every case, and by drainage of the presacral space.

*Bladder:* The sixteen cases with perforations of the bladder were all in the pelvicabdominal group. The involvement was nearly always extraperitoneal, and the structure most often injured concomitantly was the extraperitoneal rectum.

Perforations were closed with two rows of sutures, the outer one being of silk. The cystostomy tube was then inserted high in the dome of the bladder so that it was well above the pubic symphysis. Suture of perforations near the base of the bladder need not always be done if they are not readily accessible. There is usually an associated extensive hematoma of the space of Retzius, often with active hemorrhage, making exposure of the bladder more difficult. When exploratory laparotomy had been performed, as was done in all sixteen cases, suprapubic cystostomy was carried out after closure of the peritoneum.

There was one patient with a rupture of the posterior urethra secondary to a crushing injury of the pelvis who died of uremia, retroperitoneal sepsis, and pneumonia.

*Liver:* Of the fifty-eight patients with liver injury, nineteen were in the abdominal group and were, in almost all cases, operated upon through a right rectus muscle-splitting incision. When it was feasible, lacerations of the liver were sutured over free omental grafts, and this satisfactorily arrested hemorrhage. Lacerations could not be sutured in two cases, and were therefore treated by packing with petrolatum gauze. Because of the possibility of leakage of bile and resultant bile peritonitis, drains should be inserted through a stab wound in the abdominal wall or flank. As a rule, lacerations of the liver caused by shell fragments were not large compared with the fractures of the liver seen in civil practice.

The large number of injuries to the liver in patients with thoracoabdominal wounds (thirty-nine cases) is to be expected because of the size and position of the organ. For the same reason, and also since it offers a barrier to missiles perforating the diaphragm, the liver was the only organ injured in twenty-seven of these cases.

In sixteen of the thirty-nine cases, no operative repair of the liver was necessary. Of the twenty-three other cases, the injury was repaired by transdiaphragmatic operation in six, and by the latter combined with laparotomy in ten. The remaining seven patients were operated upon through the abdomen, since the thoracic injury did not require thoracotomy.

In combined thoracolaparotomy through the same incision, exploration and repair of the liver were carried out through incisions in the flank (two cases), upper quadrant of the abdomen (three cases), or through a kidney incision ex-



tended to the flank (two cases). In four of these thoracoabdominal cases lacerations were packed with petrolatum gauze.

Postoperative transdiaphragmatic biliary-pleural fistula is an important complication in these cases. In order to avoid this as far as possible tight closure of the diaphragm with nonabsorbable sutures plus transperitoneal drainage (accomplished through a stab wound of the abdominal wall) should be used for all but small liver wounds.

*Spleen:* The spleen was injured in twenty cases, fifteen of them in the thoracoabdominal group. In nine of the latter, transdiaphragmatic splenectomy was performed, and in three the spleen was removed at laparotomy. Trans thoracic splenectomy is more easily performed than splenectomy by the trans abdominal route. The spleen was not removed in the three remaining cases since the injury was minimal. Splenectomy was performed in all five cases of splenic injury in the abdominal group. The operative mortality rate in these twenty cases was 15 per cent, that for splenectomy was 18 per cent.

*Kidney:* Operative procedures upon the kidney were necessary in only sixteen of the twenty-seven patients in whom this organ was injured. In ten suture of the kidney was performed, usually over muscle grafts, and in six, nephrectomy was carried out.

Exposure of the kidney for repair or nephrectomy was always made through a lumbar incision. When indicated, the peritoneum was opened so that other structures could be examined. In the event of intraperitoneal lesions demanding operation first, the extent of the injury to the kidney was determined. Subsequently, the peritoneum closed over the wound of the kidney, and, if further operation was to be done through a lumbar exposure, drainage of the perirenal space was provided through a lumbar stab wound. Injury to the kidney producing a unilateral hematuria frequently requires no immediate operation, especially in the presence of more urgent abdominal surgery.

Decision to perform nephrectomy is made only when very extensive injury to the kidney or its pelvis is present. Chemotherapy and transfusions have greatly lessened the danger of postoperative renal sepsis and secondary hemorrhage which were so commonly encountered in World War I.

*Ureter:* There were three patients who sustained injuries to the ureter resulting in urinary fistula, with no postoperative deaths.

*Pancreas:* One patient in the abdominal group, with a wound of the pancreas, died postoperatively with extensive fat necrosis and chemical peritonitis.

In the foregoing discussion of injuries to specific organs, the operative mortality rates listed are those for all patients with lesions of the particular viscus, whether it was injured alone or in combination with other organs.

*Anesthesia:*—The anesthetic agent employed in nearly all major operative cases was a mixture of nitrous oxide, oxygen, and ether, usually administered through an endotracheal tube. Use of the tube provided better muscular relaxation, especially in upper abdominal operations, and better oxygenation and control of respiration, which were especially important during thoracotomy. Furthermore, at the end of operation, tracheobronchial secretions could be

aspirated, an important factor in keeping pulmonary complications at a minimum. The open circuit was preferred to the closed circuit since it provided better oxygenation.

In a few cases, general anesthesia was supplemented by abdominal wall block, with procaine to provide better relaxation without the necessity of deep anesthesia. In such cases, infiltration of the peritoneum with procaine solution facilitated closure of the wound.

Major operations were performed under local procaine infiltration. Spinal anesthesia was not employed.

Of the anesthetic agent did not seem to contribute to shock. In fact, in some patients, especially those in the thoracoabdominal group, seemed to improve. Anesthesia had been induced. However, turning the patient on his side or operating to perform thoracotomy or debridement of wounds was often associated with a fall in blood pressure.

Patients in poor condition at the end of operation were left on the table for an hour or more whenever possible while transfusion and oxygen therapy were continued. While it is true that the mortality rate is higher in cases with a longer operating time, little significance can be attached to this factor, especially in view of the extent of the injuries in such cases.

#### POSTOPERATIVE MANAGEMENT

All patients with chest and abdominal wounds were treated in a special postoperative ward under the supervision of a full-time medical officer. While the importance of expert postoperative care cannot be overemphasized, space permits mention of only the salient features.

Oxygen therapy was often required for as long as three to five days, especially in thoracoabdominal cases. Distention was instituted almost routinely in cases with peritonitis, and continued until a positive fluid balance had been achieved and peristalsis had resumed, that is, for an average of three to four days.

Totally 3,000 c.c. of intravenous fluids and 250 c.c. of plasma were given daily as long as indicated, and in addition about forty per cent of these patients required one or more blood transfusions.

Intramuscular penicillin therapy in doses of 20,000 units every four hours was continued in all patients for seven days or longer if they were still febrile. Most patients in the pelvicabdominal group received this dose every two hours for seven to ten hours because of the supposed danger of gas bacillus infection, which, however, developed in only one case. Sulfadiazine therapy was instituted for over one-fourth of the patients in the pelvicabdominal group for the same reason, and in any case where pulmonary complications were evident or seemed likely to occur. Routine administration of sulfadiazine was not carried out.

Precautions for the prevention of atelectasis were taken. In patients with closed intercostal catheter drainage, the catheter was kept patent until its removal, usually forty-eight hours postoperatively, and 40,000 units of penicillin in saline solution were then injected intrapleurally. In those with

bile in the pleural fluid or gross contamination of the pleural cavity, drainage was continued for three days or longer. Thoracentesis was often necessary one or more times to remove reaccumulations of serosanguineous fluid.

Colostomy openings were made in exteriorized segments of bowel twenty-four to forty-eight hours postoperatively and were enlarged the next day. The colostomy usually began to function by the fourth or fifth day.

In general our policy was to hold post-thoracotomy patients for at least seven days and post-laparotomy patients for ten days or longer. It was, therefore, possible to keep patients until they were in good condition and could be safely evacuated.

#### POSTOPERATIVE COMPLICATIONS

Shock was one of the chief causes of death and it will be discussed in the section on postoperative deaths.

The commonest abdominal complication was ileus (twenty-three cases). The clinical diagnosis of some important degree of peritonitis was made in fifteen cases, two of which were due to bile in the peritoneal cavity. Definite retroperitoneal sepsis was present in eight cases in the pelvic/abdominal group.

Other abdominal complications included: gastric fistula (1 case), duodenal fistula (2), jejunal fistula (1), fecal fistula (5), urinary fistula (8), partial wound dehiscence (2), wound sepsis about the colostomy (6), gangrene of exteriorized colon (1), prolapse of small intestine through the colostomy wound (1), and considerable sepsis of the wound of entrance in the buttock (4).

Infection of the operative wound of moderate or severe degree was present in eleven patients (4 per cent of major operations).

Pulmonary complications were frequent and included thirty cases of post-operative atelectasis, frequently concomitant with bronchopneumonia (26 cases), bronchitis (6 cases) and lobar pneumonia (3 cases).

The other pulmonary complications were as follows: pulmonary edema (6), bile in the pleural fluid (6), biliary drainage from the chest wound (2), empyema (4), tension pneumothorax (2), bronchopleural fistula still present on evacuation (1), pulmonary hemorrhage (2), gangrene of one lobe of the lung (1), and small pulmonary abscess (1). In addition, several patients had some degree of hydropneumothorax on evacuation, and probably some cases of non-reexpanded lung and empyema became evident after they had left our hands.

Uremia occurred in five patients. It was thought to be due to reflex anuria in two of them, to urinary extravasation and retroperitoneal sepsis in two others, and to a severe transfusion reaction in the fifth case.

Transfusion reactions due to the use of stored type O blood were all too frequent (nineteen patients). Several had temporary oliguria due to hemoglobinuric nephrosis, along with prolonged hypotension.

Miscellaneous postoperative complications included thrombophlebitis of the iliac and femoral veins (2), prolonged paroxysmal auricular tachycardia (1), pyelitis (2), meningitis (1), toxic psychosis (3), and infection of the entrance wound in the buttock with gas-forming organisms (1).

## POSTOPERATIVE DEATHS

*Abdominal Group*—There were twenty-seven postoperative deaths in the abdominal group, the principal causes being hemorrhagic shock (8 cases), traumatic shock (6), peritonitis (8), and postoperative pulmonary complications (4). In practically all cases two or more of these factors were present, and it was often difficult to be sure which was the most important.

All of the eight patients who died of hemorrhagic shock had perforations of the intestinal tract with marked hemoperitoneum, and in four visceral injury was severe. All died within nine hours after surgery and four of them died on the operating table. The interval between wounding and surgery varied from eight to seventeen hours, and probably most of these patients were in irreversible shock on admission. Each had received from 1,000 to 4,000 c.c. of blood before and during surgery.

Death from traumatic shock due to severe associated injuries occurred in three patients, two of whom had no significant intra-abdominal damage. Shock was due to severe abdominal injuries in two other cases, and to marked blast injury of the chest and abdomen in the sixth case. All of these patients died within twenty-four hours of operation.

Of the eight patients who died with peritonitis, multiple intra-abdominal injuries were present in four, and intestinal resection and anastomosis had been performed in two of these. Three patients also developed serious pulmonary complications postoperatively. In six cases some degree of peritonitis was present at operation, the average time lag being twenty-eight hours. In one of these patients, already wounded forty-eight hours, the only operation was drainage of the peritoneal cavity. In the other two cases the time interval was only nine hours, and peritonitis was due to surgical errors. Suture of the intestine for multiple perforations was carried out in a 12-year-old girl in poor condition, who resection should have been done because of contusion of the bowel wall in the injured segment. The other patient developed a gastric fistula and peritonitis, due either to inadequate closure or to a missed perforation.

Respiratory complications were the chief cause of death in four patients. Two deaths, within six hours of operation, were believed to be due to aspiration of vomitus and pulmonary edema. Another patient died of massive pulmonary collapse, and the fourth had a severe tracheobronchitis with profuse tenacious sputum, not relieved by bronchoscopy.

Another 12-year-old girl, with a partial cord transection thirty-six hours old on admission, died of ascending meningitis due to Friedländer's bacillus eight days following laminectomy and nephrectomy.

*Pelvicabdominal Group*.—Associated injuries were severe in seven of the eleven patients in this group who died postoperatively. Fractures of the pelvis were present in five cases, gangrene of the leg in two, and thrombosis of the external iliac vein in another. In only one case, however, was traumatic shock thought to be the chief cause of death.

While there were no deaths due to peritonitis, two were due to severe retroperitoneal sepsis, resulting from a severe laceration of the extraperitoneal rectum in one case, and of the posterior urethra in the other.

Pulmonary complications were the ultimate cause of death in four cases (atelectasis in two, bilateral pneumonia in another, and a probable pulmonary embolus from a thrombosis of the iliac vein in the fourth).

Three patients died of uremia, two of whom also had pulmonary complications (pulmonary infarcts in one case and bilateral blast damage in the other).

The uremia was thought to be due to reflex anuria in a patient with thrombosis of the iliac vein, to a transfusion reaction in another, and to transfusion reaction complicated by sulfadiazine overdosage in a third.

The eleventh patient, who had a severely fractured pelvis with retroperitoneal hematoma, died on the tenth day of hemorrhage from several acute gastric ulcers.

*Thoracoabdominal Group*—Shock was the principal cause of death in seven of the twelve postoperative deaths in this group. Three of these occurred at operation and four on the day of operation. Hemorrhagic shock was prominent in four of these patients (one of whom died of massive pulmonary hemorrhage) and traumatic shock in the other three.

Pulmonary complications were the chief cause of death in four other patients who died on the fourth, sixth, and eighth postoperative days. Three of these had empyema, one of whom had gangrene of one lobe of the lung, and another a bronchopleural fistula and bilateral bronchopneumonia.

The eleventh patient died with bile peritonitis, and uremia of undetermined origin, one week after nephrectomy.

In summary, the chief causes of death in the fifty patients who died postoperatively were as follows (the figure in parentheses indicates the number of cases in which the complication was an important secondary cause of death): hemorrhagic shock, 12 (9), traumatic shock, due predominantly to abdominal injuries, 4 (30), traumatic shock, due primarily to associated injuries, 6 (1), peritonitis, 8 (3), retroperitoneal sepsis, 2 (1); pulmonary complications, 12 (11), uremia, 4 (1), and others, 2 (2).

#### SUMMARY AND CONCLUSIONS

1 The clinical findings, surgical management, and results obtained in the treatment of 335 casualties with abdominal injuries have been presented.

2 In 330 of these patients operation was indicated, but the poor condition of 27 precluded operation. Fifty of the patients operated upon also died, giving a total mortality rate for unoperated and operated cases of 23.0 per cent.

3. Three hundred three patients were operated upon, an operability rate of 91.8 per cent, and the fifty postoperative deaths represent an operative mortality rate of 16.5 per cent.

4 Associated injuries were present in 55 per cent of the cases, and were an important cause of morbidity and mortality.

5. Abdominal injuries have been classified into abdominal, pelvioabdominal, and thoracoabdominal groups, and the clinical significance of this classification has been pointed out.

6. The principal cause of death was shock, the result of hemorrhage or severe injury. The condition of the patient on admission and the extent of his injuries and blood loss were the best guides to prognosis. Infection and late deaths from peritonitis were not common and if the patient survived the first forty-eight hours after operation the chance of recovery was good.

7. The chief factors acting to increase the operability rate and to decrease the mortality rate in patients with abdominal wounds in World War II were more rapid and efficient evacuation, better supportive therapy with blood and plasma, improved anesthesia, sulfonamide and penicillin therapy, and improved surgical methods.

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## PERFORATED GASTRODUCODENAL ULCER

A. LA MONT BARTILL, M.D., OAKLAND, CALIF.

(From the Department of Surgery, Permanente Foundation Hospitals,  
Oakland and Richmond, Calif.)

### INTRODUCTION

THERE are few instances in the natural course of events when man may rescue his fellow man from certain death. One of the commonest of such instances in medical practice is in the case of an acute perforation of a gastroduodenal ulceration. The purpose of adding further to the already voluminous, although somewhat outmoded, literature on this subject, is to show that, for the first time the certainty of saving such a patient is even greater than the certainty of his dying if untreated. Up to the present time, there are only two reports in the literature, those of Graham<sup>1, 2</sup> and Tilton,<sup>3</sup> of significant groups of treated patients with acute perforations, with the low mortality which can and should be achieved by all surgeons. These two groups are both small and include very favorable material.

The principles and method of treatment of this abdominal catastrophe which will accomplish such a low mortality are all well known but seem to fail to be properly correlated and applied at the same time and in all cases. The reported mortality rates of from 10 to 25 per cent of operated patients with acute perforations are inexcusably high and can only reflect a failure of surgeons everywhere to apply what is known in the treatment of this emergency, and to do so in every case with the expectation that almost no patient with a perforated ulcer should die if he is seen before he becomes moribund.

This report includes a series of eighty-eight consecutive patients operated for perforated gastroduodenal ulcers in this hospital in the three-year period since the first admission for this illness, together with the data on thirteen patients who were not operated. Thus, every patient who has ever entered this hospital with such a perforation is included. Of the operated patients there was only one death, a mortality rate of 1.1 per cent, and this one death was from extrabdominal causes. A brief comparison is made with other published statistical studies. A more detailed correlation of mortality in relation to various categories such as age or duration of symptoms is superfluous in a group of cases with so low a death rate. The breakdown of statistics is offered in our group of patients chiefly to demonstrate that the mortality risk in them is in every way comparable to other reported series. The number of operated patients is sufficiently large to be significant. There is no reason to believe that the mortality should be any greater in our next hundred patients, if we should have the ill luck to have twice the number of deaths in the next group the over-all mortality would still be in marked contrast with the current figures. A somewhat detailed outline of our principles of treatment is in-

cluded in order that they may be more generally adopted in an effort to reduce the mortality rate for people with perforated ulcers. It is fully recognized that there is little which in itself is new or even unusual in this treatment. Rather, it is felt that it is the correlation and utilization of all of the best principles in every instance which has resulted in a new and unusually low mortality rate. It is further emphasized that these principles are so simple and easily applied that this mortality rate should be the prevalent rather than the uncommon one.

#### ANALYSIS OF MATERIAL.

As has already been indicated, the principal reason for analyzing our material in regard to the various factors normally affecting mortality risks is to demonstrate that our group of patients in no way differs from other reported series in this regard. There are a few interesting additional data, particularly those relating to the incidence of this condition. Comparisons are made with DeBakey's collected series.\*\*

*Incidence.* Our figures in regard to the incidence of perforation of gastric and duodenal ulcers are particularly valuable, because all of our perforations come from a known aggregate of population of a known type, and because the ratio of perforations to other hospital admissions is similarly accurate in that such admissions are entirely unselected and represent all hospital admissions for the same definite group of people.

The population from which these cases are drawn consists entirely of skilled and unskilled working people in heavy industry under wartime conditions of work and housing. It is safe to say that all of the perforations occurring in this known group during the three year period have been treated by us. It is to be noted that this group differs from a peacetime group of heavy industry workers in that there were more people in older age groups and more who were physically disqualified from military service and thus had a higher incidence of chronic illness such as peptic ulcer.

When related according to the number of perforations in relation to the average number of persons under our care, there were 31.08 perforations per 100,000 of population per year.

In relation to hospital admissions, excluding admissions for industrial accidents, there were five perforations per 1,000 admissions, or 0.50 per cent of all admissions were for perforated ulcer. This is much higher than is generally reported.\*

*Sex.*—There were three females in this series, or 2.93 per cent of the total. The average ratio of males to females under our care was 3.31 to 1. Thus the figure 2.93 per cent may be adjusted to 9.70 per cent of females to males suffering from perforated ulcers, correcting for the differential in the numbers of males and females from which our patients were drawn. This is considerably higher than the usual ratio reported in the modern literature; and, although the figure is too small to be of definite numerical significance, one may speculate that women may perforate ulcers more commonly if placed in similar working situations with men.



*Previous Symptoms.*—Fifty-seven, or 64.8 per cent, of these patients had a history of symptoms indicative of peptic ulcer. This is a somewhat lower figure than DeBakey's\* reports in his collected series (85.1 per cent) or his Charity Hospital series (75.3 per cent). In addition, a considerable number of those with positive histories had been having symptoms only a short while before their perforation. Possibly, there were more perforations of acute ulcers of short duration in our group than the average, or, more likely, there were more hyposensitive individuals in the group.

*Previous Perforations.*—Six, or 6.8 per cent, of these patients had one or more previous perforations. Conn reported twelve re-perforations in 300, a rate of 4 per cent, at the San Francisco County Hospital.<sup>7</sup> The rate of re-perforation is no doubt increasing commensurate with the rapid increase in the incidence of perforation generally.

*Age.*—There is little doubt that age of the patient is fully as important as the preoperative interval in determining the mortality rate among the published series. This is well demonstrated by the reports of DeBakey and Odum,<sup>8</sup> Barber and Madden,<sup>9</sup> Kelly,<sup>9</sup> and others. Our age distribution is seen in Table I.

TABLE I. AGE DISTRIBUTION IN EIGHTY EIGHT PATIENTS OPERATED FOR PERFORATED PEPTIC ULCER

AGE	NUMBER PATIENTS	PER CENT PATIENTS
Under 20	0	0.0
20-29	12	13.6
30-39	24	26.1
40-49	26	29.5
50-59	19	21.6
60-69	7	8.0
70-79	1	1.1

DeBakey's collected series\* showed that 4 per cent of reported perforations occur in the first and second decade, 73.1 per cent in the third to fifth decade, and 22 per cent past the age of 50. Our patients were in a significantly older age group, over 80 per cent being 50 years old or older.

TABLE II. TABULATION OF EIGHTY EIGHT PATIENTS OPERATED FOR PERFORATED ULCER ACCORDING TO TIME ELAPSED BETWEEN PERFORATION AND SURGERY WITH COMPARISON TO THE COLLECTED SERIES<sup>10</sup>

HOURS ELAPSED	OUR SERIES			COLLECTED SERIES	
	NUMBER PATIENTS	PER CENT PATIENTS	MORTALITY	PER CENT PATIENTS	PER CENT MORTALITY
0-6	34	38.63		50.83	16.5
6-12	37	42.01		31.62	21.1
12-18	13	14.77		7.03	38.5
18-24	2	2.27		1.43	62.4
Over 24	2	2.27		13.66	61.5
All Cases	94	100.00	1.1	100.00	34.4

*Preoperative Interval.*—From the data in Table II it is readily seen that our group is also more unfavorable than is the average in DeBakey's collected series in regard to time elapsed between perforation and treatment. This is particularly true of the group under six hours. It is also true, however, that we have had much fewer perforations over twenty-four hours than the average.

of the collected series. Our one mortality was a 49-year-old man who had been perforated fifteen hours before surgery. As will be detailed later, he died of heart failure, so that neither age nor time had any bearing upon his death.

*Peritoneum.*—Forty-eight, or 58.5 per cent of the eighty-two patients who had films taken, demonstrated roentgenologic evidence of pneumoperitoneum preoperatively. We believe that more careful technique in keeping the patient in proper position for a longer while before taking upright and lateral films would have resulted in a greater number of positive films. However, we do not feel that x-ray evidence is of sufficient value, except in the rare diagnostic problem, to waste time or further burden the patient by a more careful technique. We would not condone the injection of air through a stomach tube in order to demonstrate a perforation, as has been advocated by some authors.

*Location of Perforation.*—As in all groups, there was some difficulty in classifying those ulcers located near the pylorus. Eight, or 9.1 per cent of the perforations were located at the pylorus. Of the remainder, nine, or 10.2 per cent were definitely gastric, and seventy-one, or 80.7 per cent were duodenal. Key placed this relationship as 38.9 per cent gastric, 51.2 per cent duodenal, and 9.8 per cent pyloric in the collected series.<sup>4</sup>

*Postoperative Complications.*—Except as a cause of death, peritonitis cannot be considered a complication of this disease, since all of these patients have either a chemical or a bacterial peritonitis or both from the start, and a startlingly high per cent of patients who have been perforated over six hours do have positive peritoneal cultures.

As in all other series, our commonest complication was wound infection. This occurred in nine instances, or 10.2 per cent of our patients. Eight of these were subcutaneous infections which healed readily, and one was a deep wound infection which healed after a prolonged period. There were no persistent sinuses, although nonabsorbable sutures were used throughout. DeBakey's collected series had 25 per cent wound infections.<sup>4</sup>

One patient suffered a complete wound separation and evisceration on his eleventh postoperative day. This was closed at once with through-and-through wound sutures under local anesthesia, and promptly healed without further difficulty.

There were four subphrenic abscesses—all drained anteriorly, three patients had a significant postoperative atelectasis, two patients developed pneumococcus pneumonia, one patient had a massive hemorrhage from his ulcer site and was treated by transfusion, and one patient began an auricular fibrillation with cardiac decompensation. All of these were treated appropriately and recovered.

*Mortality Rate.*—In this group of eighty-eight patients operated upon, there was one death, a mortality rate of 1.1 per cent, which is the lowest published for significant numbers of patients with this condition. A glance at Table III will demonstrate the contrast of this mortality with that apparently prevalent in the large hospitals and clinics throughout the country. Tilton's<sup>2</sup> and Graham's<sup>1,2</sup> reports were admittedly of a low mortality risk according to the

TABLE III MOST RECENTLY PUBLISHED MORTALITY RATES FOR PERFORATED PEPTIC ULCER

AUTHOR	YEAR	NUMBER CASES	PER CENT MORTALITY
Baritell, A. L.	1946	88	11
Tilton, B. J.	1936	52	10
Graham, R. R.	1938	62	12
McClure, R. D.	1940	91	17
Estes, W. L., and Bennett, B. A.	1944	80	37
Black, R. M., and Blackford, R. E.	1945	93	120
Barber, R. F., and Madden, J. L.	1943	86	128
Hartzell, J. B., and Soreck, M. L.	1939	39	129
Marshall, S. F., and Keleher, P. C.	1940	46	130
Raw, S. C.	1944	312	144
Cohn, R.	1941	300	150
Berson, H. L.	1942	151	152
Ross, J. C.	1940	175	160
Paletta, F. X., and Hill, W. R.	1943	83	169
DeBakey, M., and Odum, C. R.	1940	211	174
Ross, A., and Letourneau, G.	1939	220	177
Donald, D. C., and Bartlett, S. M.	1942	116	185
Meade, R. H.	1943	68	191
Timoney, F. N.	1943	246	195
Griswold, A. R., and Antonie, R.	1941	102	196
Falk, L. S.	1933	100	200
McCreery, J. A.	1938	170	205
Eliaeson, E. L., and Thigpen, G. M.	1938	70	214
Sangster, A. H.	1939	400	230
O'Donoghue, J. B., and Jacobs, M.	1942	200	246
McCabe, E. J., and Merzheimer, W.	1943	87	252
Martz, H., and Foote, M. H.	1940	50	260
Parker, E. F.	1941	52	270
Davidson, T. C., and Rudder, F. F.	1940	155	280
Thompson, H. L.	1939	424	287
Hartzell, J. B., and Soreck, M. L.	1939	234	290
Reed, J. C.	1938	100	300

usual standards. It is probable that the mortality has been even higher in the hands of the casual surgeon who sees only an occasional perforated ulcer. It has already been shown that our group was not more favorable material than that reported in other series. However, it is acknowledged and hoped that mortality rates in the last three years, not yet reported, will be much lower than they have been for the preceding twenty years.

This can be expected on the basis of the use of chemotherapy and the utilization of all of the basic surgical principles already known, in every case of perforated ulcer. Surgeons who persist in advocating such proved unsound principles as drainage of the peritoneum or adding accessory procedures to simple closure may expect to continue to lose every fifth or sixth patient.

It is unfortunate and a stimulus to ourselves not to relax our constant vigilance and best efforts for these patients that our one death was preventable. This patient was 49 years of age and was operated fifteen hours after his perforation had taken place. He was known to have rheumatic heart disease with mitral stenosis. Twenty-four hours postoperatively he developed acute pulmonary edema and died in an hour despite rapid intravenous digitalization, aminophylline, hypertonic glucose, morphine, and atropine, 95 per cent oxygen, and tourniquets. Autopsy confirmed the cause of death. It is believed that more judicious administration of fluids postoperatively would have prevented this catastrophe.



diagnostic problem may require more time, but there is little to be gained and much to be lost in wasting time on a patient who is certainly going to require laparotomy anyway.

We do not advocate the placement of a gastric suction tube conservatively, but do not condemn it. We feel that the retching which may result in greater soiling of the peritoneum and that the passage of such a tube through the mouth or nose and pharynx with the perforation still open must carry down further organisms which have access to the peritoneum. If the patient is to be treated conservatively or if delay before surgery is necessary, continuous suction should be instituted at once.

Soutter<sup>17</sup> and others have shown that true shock is rarely a part of the picture of a perforated ulcer in the absence of other causes. Time need not be lost in treating the appearance of shock when it is not present. We feel that the intravenous administration of 5 Gm. of sulfadiazine in 500 c.c. of  $\frac{1}{2}$  per cent sodium lactate should be begun in the emergency room or the operating room in all instances of peritonitis.

**Anesthesia**—It has been repeatedly shown that spinal is almost always the anesthetic of choice, and such is our routine. In the face of the usual contraindications for spinal anesthesia or the patient's refusal of such anesthesia we have found that intravenous Pentothal with local anesthesia is well tolerated by these patients.

**Operative Method**—The incision should be short.<sup>18</sup> Exposure is adequate through an 8 to 10 cm. incision which may be either rectus abdominis or transverse. Small incisions are important because these patients are prone to develop wound infections and separations.

The perforations are generally readily apparent on the anterior surface of the stomach or duodenum. All gastric ulcerations should be biopsied, and even though the biopsy is benign, the patient should be followed postoperatively with the same suspicion as the gastric ulcer patient who is perforated. He should be subjected to gastric resection for the customary indications. One of our patients had a negative biopsy from a perforated gastric ulcer but was lost from our clinic postoperatively until he returned one year later and was explored for an inoperable carcinoma of the stomach.

The next step is closure of the perforation. This may be done with a single row of interrupted Lembert sutures of cotton placed in the longitudinal axis of the bowel with a tag of fat tied over these. Purse strings or multiple layers of closure are unnecessary, tend to obstruct the lumen of the bowel and generally are tied in such a manner as to cut through or necrose tissue by pressure.

The one very definitely new and valuable contribution we have made in regard to surgical technique is the method of closure which we have developed and advocate very strongly in the presence of edema and inflammation about the site of perforation. The difficulty of obtaining a satisfactory closure under these circumstances is well known and has led to the ingenious method described by Glatch and Owen.<sup>14</sup> When the customary closure is accomplished

under such conditions there is danger of obstruction. Perhaps less appreciated but more important is the danger of the sutures cutting through, or of sufficient necrosis of tissue due to their tension to allow further leakage to develop. These difficulties are entirely avoided by the very simplest of methods which we have used with complete success in twenty instances. To our knowledge, no regular use of this method has ever been described, although several authors make brief mention of occasional use of what seems to be the same means of closure.<sup>22 23 24</sup>

Jenn<sup>19</sup> in 1891 first suggested the use of a portion of the greater omentum as a protection in operations on the hollow viscera. In 1896, Bennett<sup>20</sup> reported the case of a perforated gastric ulcer closed by an omental plug into the perforation with recovery.<sup>21</sup> It has long been our practice in the presence of much edema or induration about a perforation, and it is now our routine, to close all perforated ulcers of the stomach and duodenum by simply tacking a tag of living omental fat over the perforation with a few interrupted cotton sutures. No attempt whatever is made actually to close the perforation, and no suture is passed through the bowel wall as Graham describes.<sup>1 2</sup> A bit of gastrohepatic omentum is usually most readily available for this purpose. The surgeon need feel no insecurity in this method. Watertight closure is entirely unnecessary. Twenty of our patients have been so treated with no complications and with the same rapid recovery as the others. This method should always be used in the presence of induration and edema.

The importance of the simplest workable procedure in closure of perforations is generally recognized, although some authors still persist in advocating such accessory procedures as gastroenterostomy, which has almost no place in the treatment of duodenal ulcer at any time.<sup>25</sup> The omental patch is certainly the simplest means of covering the perforation which is surrounded by a large area of induration.

All fluid should be sucked from the peritoneum, giving particular care to the spaces about the liver, the right gutter, and the pelvis. The abdominal cavity is closed in layers with interrupted cotton sutures. No drains are placed either in the peritoneum or the wound. The former is not only utterly useless but may be harmful, while the latter is probably of little value, since 90 per cent of our wounds healed per primam. We would offer no criticism of drainage of the wound, however, in the presence of obvious suppuration. The entire operative procedure should not require over an hour and is usually much less.

**Postoperative Care.**—Immediately on return from the operating room, the patient has a nasal tube passed into his stomach, to which continuous suction is applied for approximately forty-eight hours. At the end of this period, if the patient has good peristalsis, the tube is clamped off for a period of four hours. If there is less than 100 cc. retained in the stomach, the tube is removed and oral intake of graduated amounts of water at hourly intervals is begun. After another thirty-six hours, the patient is given fluids as desired and placed on a graduated soft diet. It is very important that the suction be kept functioning while it is in place, and this requires constant observation and care. The tube invariably becomes obstructed and needs opening up or

replacement. The suction apparatus may develop leaks or become plugged up. Failure to keep continuous suction working the first twenty-four hours may result in disaster.

The routine postoperative fluids consist of 2,000 c.c. of 5 per cent glucose in saline, 1,000 c.c. of 5 per cent glucose in water, and 500 c.c. of  $\frac{1}{6}$  molar sodium lactate administered intravenously daily. This is varied according to individual needs. Intravenous amino acids are given to older patients, those in poor nutrition, and those who have a more severe bacterial peritonitis. As fluids are begun by mouth, the intravenous administration is gradually discontinued. Sulfadiazine is administered intravenously and then orally in doses sufficient to maintain levels of 8 to 12 mg per cent. No penicillin has been used.

The use of sulfonamides in the contaminated peritoneum and wound has been entirely discontinued.<sup>21</sup> In a considerable group of patients so treated, including a significant number with perforated appendicitis, we have had no deaths. Although our mortality rate in those patients who had intraperitoneal sulfonamides was fully as good as our present rate, there were certain undesirable complications which have led us to discontinue the local use of these drugs entirely. This will be reported more fully in the future.

All of our postoperative patients except those with bacterial peritonitis are allowed early ambulation. This also applies to perforated ulcers, although the process of getting them out of bed is not applied quite so strenuously on the first two postoperative days as with other patients. We feel that this program has markedly reduced postoperative complications, particularly pulmonary and thromboembolic, has reduced the hospital stay, and has shortened convalescence. If nonabsorbable suture material is used, there should be no increased danger of wound separation.

#### CONCLUSIONS

1. A group of eight-eight patients has been operated for perforated gastric and duodenal ulcers with a mortality rate of 1.1 per cent.

2. This series is in every way comparable to other groups reported in regard to mortality risk.

3. A new, or at least heretofore unpublicized, technique of operative treatment, consisting of applying an omental patch to the perforation without any attempt at closure, has been applied to twenty patients with uniform success. It is now our routine in all cases and is strongly recommended in any patient in which there is marked edema or induration about the perforation.

4. The combination of organized teamwork in the rapid diagnosis and institution of definitive therapy in surgical emergencies together with the use of chemotherapy and the application of sound, well-recognized, surgical principles has resulted in a very low death rate for a disease which heretofore carried a formidable mortality rate. We believe that similar results could be obtained more generally.

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## INTUSSUSCEPTION OF EXCLUDED DISTAL ILEUM WITH SPONTANEOUS EXPULSION PER ANUM OF SEQUESTERED INTUSSUSCEPTUM

EDWARD O. FINESTONE, M.D., NEW YORK, N. Y.

(From the Surgical Service of Dr. John H. Garlock at the Mount Sinai Hospital)

FITZWILLIAMS,<sup>1</sup> in 1908, reported 1,000 cases and in 1921 Perrin and Lindsay<sup>2</sup> reported 400 cases of intussusception without a single instance of slough with spontaneous recovery.

Garlock<sup>3</sup> stated that intussusception of the excluded terminal ileum was discovered inadvertently in two cases in which ileocolic resection was undertaken as a second stage operation for terminal ileitis.

A review of the literature for the past twenty years discloses a small number of cases<sup>1, 5, 12</sup> wherein a spontaneous cure resulted following the expulsion per anum of the sequestered intussusceptum. However, in only one instance<sup>1</sup> has a condition somewhat similar to the present one been reported. In that case ileocolic invagination developed after the section and exclusion of the distal ileum with ileotransverse colostomy, but the condition was not relieved spontaneously. In this case, reported by d'Allaines and Martin,<sup>5</sup> the first stage operation consisted of an ileotransverse colostomy with exclusion of the distal ileum for a carcinoma of the hepatic flexure of colon. On the third post-operative day the patient developed fever, colic, and frequent diarrheal stools with passage of blood and mucus. Six weeks later, in spite of progressive weight loss and cachexia, the second stage was performed. At this operation the invagination was discovered. The specimen resected consisted of the last 30 cm. of ileum, the right colon, and part of the transverse colon. 14 cm. of the ileum had become invaginated within the excluded loop.

Treves<sup>12</sup> explained the pathologic process of spontaneous recovery in two ways. Adhesions form between the peritoneal surfaces of the entering portion and the ensheathing portions of the intestine. If a separation takes place first at the end of the middle layer, the intussusception will straighten out at the apex. Later, as separation takes place in the middle layer near the entering portion of the intestine, the section will be passed with its peritoneal layer outermost. If the separation takes place at the two ends of the middle layer in the reverse order, the section will be passed with the mucous surface outermost. The former is the common one, and the latter with the intestine turned inside out is relatively rare. The intestine in all cases is gangrenous and macerated.

### CASE REPORT

*History.*—E. R., a 48 year old white woman, was first seen in 1940, complaining of recurrent attacks of abdominal cramps associated with nausea, vomiting, and diarrhea. She had had a left salpingo-oophorectomy fifteen years previously followed by menopause; she had had a left ureterolithotomy six years previously. Since this latter operation she suffered mild frequency, urgency and dysuria associated with albuminuria and pyuria.

After a very thorough examination in the Consultation Clinic at the Mount Sinai Hospital, it was concluded that the patient was suffering from ulcerative colitis, right nephrolithiasis, double left kidney, trigonitis, and urethral caruncle.

*First Admission.*—The patient was first admitted to the Mount Sinai Hospital on March 24, 1940, and discharged on April 27, 1940. She was admitted chiefly because of a nutritional problem, since she weighed only 93 pounds and was 65 inches tall. The urinary symptoms had been minimal since the ureterolithotomy. Since June, 1939, she had had recurrent attacks of abdominal cramps, nausea, vomiting, diarrhea, and fever. These acute attacks lasted about one or two weeks and recurred almost every month.

Sigmoidoscopy revealed a normal rectum and sigmoid, but there was blood and mucus coming from above, where a lesion was presumed to exist. Repeated x ray studies revealed a normal esophagus and a ptosed stomach, with no evidence of organic intrinsic lesion. The ileocecal bulb was dilated but complete with no irregularities in outline. The small bowel as studied at short intervals and showed no abnormality in the jejunum or proximal ileum. The terminal three inches of ileum showed distinct irritability. It was distensible yet tended toward an inconstant narrowing. The right half of the colon was distended, revealed gas in the preliminary examinations, and showed marked loss of haustrations. The appearance suggested the likelihood of an inflammatory process involving the terminal ileum and probably the colon also. Preliminary x ray examination showed irregular calcifications in the right upper quadrant in the region of the right kidney.

During this hospital stay the patient was seen by several consultants who concluded that operation should not be done, because there was insufficient evidence of organic change in the bowel. The patient was thought to be a very nervous and hysterical type, so that treatment was directed toward the malnutrition, anitoxinosis, and diarrhea. By means of a carbohydrate diet, large amounts of all vitamins parenterally, neoprostol, and spasmalgin, she showed progressive improvement. Weight increased from 93 pounds to 100 pounds and stool diminished from eight to three a day.

*Second Admission.*—Shortly after the patient's discharge from Mount Sinai Hospital, there was a recurrence of the cramps, diarrhea, and loss of weight. She was readmitted on Feb. 22, 1941, and discharged on April 12, 1941. During this stay she was found to be pale, markedly underweight, and dehydrated. The cecum could be rolled under the fingers with only slight tenderness. Otherwise the abdomen was negative.

X ray views of the chest revealed calcified areas in the left apex due to an old tuberculous process. New roentgenograms of the intestines revealed considerable loss of haustration of the entire colon with numerous constricted areas. The terminal ileum was similarly involved, suggesting a diffuse inflammatory process. Blood showed hemoglobin, 90 per cent, 100 cells, 13,000 with a normal differential. Sedimentation rate was 11/4 hours. Wassermann reaction was negative. Blood calcium was 11.2 mg and phosphorus 3.6 mg, phosphatase was 65 King Armstrong units, sugar 125 mg, chlorides 560 mg.; blood sodium 133.7 mEq per liter. Urine contained a trace of albumin, a rare red blood cell, and a moderate number of white blood cells. Stool was negative. Basal metabolic rate was plus 17 per cent. Electrocardiogram showed a low T<sub>1</sub>, ST transition in II, and III slightly depressed. Renin test meal gave normal results, Frei, negative.

It was now felt that the bowel symptoms were attributable to organic changes and accordingly an ileosigmoidostomy was performed. At this operation the terminal ileum, the cecum, ascending colon, and proximal transverse colon were found to be the site of a chronic inflammatory process. The terminal ileum about 16 inches from the ileocecal junction was divided, both ends inverted, and the proximal loop anastomosed laterally to the sigmoid. The mesentery of the ileum had been widely divided at the site of exclusion of the terminal ileum, but no attempt had been made to suture it. The patient had a rather stormy postoperative course, but then showed progressive improvement until discharge.

*Third Admission.*—About two weeks following her discharge from Mount Sinai Hospital, the patient developed intestinal obstruction characterized by abdominal cramps, vomiting, and constipation. She was admitted to another institution where this diagnosis was confirmed by roentgenograms, showing small bowel loops distended with gas and fluid levels.

A Miller Abbott tube was successfully passed and the patient was discharged. The tube was in place for two weeks when she was readmitted to the Mount Sinai Hospital on May 12, 1941, and discharged on June 3, 1941. A tender mass was felt in the right lower quadrant of the abdomen. After adequate desiccation of a very fine Miller Abbott tube was passed through the Miller Abbott tube to pass through the slow growth of the tumor. Because of a very extensive scar the obstruction was removed, the Miller Abbott tube was removed. The patient continued to take food by mouth and pass stool per rectum. There was no further evidence of obstruction. Intermittent diarrhea appeared on several occasions. When she left the hospital there was some edema of the legs.

Follow-up at the clinic on Sept. 4, 1941, showed that the patient's general condition had improved markedly. She had gained twenty pounds. The wound was well healed. Bowels moved three or four times a day. On May 14, 1942, the patient was well and had gained twenty-five pounds in all since the original operation. She still complained of intermittent pain in the right lower quadrant where a mass seemed to be felt.

Fourth Admission—Winter 1941 when the abdominal discomfort was just about the same. She had several episodes of intestinal obstruction successfully relieved by the use of the Miller Abbott tube. In the latter part of May, 1942, she showed just another such episode which did not respond very well to intubation. Therefore, she was admitted to the Mount Sinai Hospital June 19, 1942, and discharged Aug. 14, 1942. During this stay she was found to be chronically ill, anemic, dehydrated, and showing evidence of marked malnutrition. With the Miller Abbott tube in place there was no abdominal distention and no abdominal tenderness in the right lower quadrant. There were three well-healed scars on the lower abdomen: (1) left ureterolithotomy, (2) exploratory laparotomy, (3) slow growth of the tumor.

On June 24, 1942, operation was carried out through a left lower paracostal incision. The end of the Miller Abbott tube was found to reach almost to the ileocecal junction, the stoma of which was satisfactory. The cause of the obstruction was seen to be due to the incarceration of a loop of small bowel beneath the free margin of the mesentery of the ileum just proximal to the caecum. The obstruction was excised and the free edge of the mesentery was sutured to the posterior parietal.

For about two weeks postoperatively the course was smooth with resumption of frequent low bowel movements. Then the patient again developed nausea, vomiting, distention, and fever. Further attempts at intubation failed. On the tenth postoperative day the lower angle of the wound was inflamed with progressive suppuration, so that it was necessary to incise and drain the wound one month following this last operation. It was found that intra-peritoneal suppuration existed as well as that in the wound. Further progress was slow and at the time of discharge from the hospital, the wound showed clean granulation with no evidence of suppuration.

Fifth Admission—The patient was at home for only eleven days when she was again readmitted, Aug. 30, 1942, and discharged, Oct. 21, 1942. On the day before this admission she suffered severe lower abdominal cramps with nausea and persistent vomiting. An enema had been fairly effective. She still appeared chronically ill and poorly nourished. The abdomen was moderately distended. A nontender immobile sausage-shaped mass was palpated in the right lower quadrant. Numerous leukocytes were found. Rectal examination revealed a small amount of stool. Hemoglobin was 60 per cent, white blood cells were 12,200. Urine contained albumin and acetone. Blood culture was sterile. An intravenous infusion was again started and an attempt was made to pass the Miller Abbott tube. The mass in the right lower quadrant became tender and the temperature rose to 100° F. Some sort of pericolic exudate was thought to exist and accordingly sulfathiazole was administered. About one week later the mass was noted in the umbilical region. The fever gradually subsided. Two weeks later, after a few days of intensely severe cramps, the patient noted a mass extruding from the rectum. This was a portion of gangrenous bowel which was completely extruded in the next twelve hours. It measured fifteen centimeters in length. Following this she felt well. In view of the disappearance of the mass from the right lower quadrant and subsequently from the umbilical region, it was concluded that the extruded

bowel was the excluded portion of terminal ileum. One week later another smaller, tender mass appeared in the right lower quadrant. This was interpreted as an inflammatory reaction about the site of the previous intussusception. Two weeks later the mass was no longer palpable. The patient was afebrile, eating well and having several bowel movements daily. A barium enema was made and the x-ray views revealed the abnormality in the colon, due to the colitis noted originally in 1940 (Fig. 1). In addition, the cecum and ascending colon failed to fill out (Fig. 2). This defect was interpreted as a result of the intussusception of the ileum, cecum, and ascending colon.



FIG. 1—Roentgenogram made with barium enema, March 15, 1940, about one year prior to operation shows evidence of colitis involving particularly the ascending and transverse colon. Note the narrowing of the terminal ileum and the position of the cecum which is missing in the view taken after operation (Ileoceceocolostomy with exclusion March 1941).

*Follow-up Record*—On Dec. 17, 1942, the patient stated that she had been remarkably well since discharge from the hospital. She had gained more than seventeen pounds. Stools were solid with occasional diarrhea, and pain in the right lower quadrant and about the umbilicus. She had had one episode of biliary colic with jaundice, both of which cleared up spontaneously. On June 17, 1943, she had gained thirty pounds since discharge from the hospital. She still complained of diarrhea with seven bowel movements a day and occasional periumbilical pain.

*Sixth Admission*—The patient was readmitted on Sept. 17, 1943, and discharged on Oct. 22, 1943, because of an incisional hernia. She had left the hospital about ten months

A Miller Abbott tube was successfully passed and the small bowel decompressed. The tube was in place for two weeks when she was readmitted to the Mount Sinai Hospital on May 13, 1941, and discharged on June 3, 1941. A tender mass was felt in the right lower quadrant of the abdomen. After adequate decompression, x-ray examination showed barium injected through the Miller Abbott tube to pass through the ileocecal junction satisfactorily. Because of x-ray evidence that the obstruction was relieved, the Miller Abbott tube was removed. The patient continued to take food by mouth and pass stool per rectum. There were no further symptoms of obstruction. Intermittent diarrhea occurred on several occasions. When she left the hospital there was some edema of the legs.

Follow-up at the clinic on Sept. 4, 1941, showed that the patient's general condition had improved markedly. She had gained twenty pounds. The wound was well healed. Bowels moved three or four times a day. On March 4, 1942, the patient looked well and had gained twenty five pounds in all since the original operation. She still complained of intermittent pain in the right lower quadrant where a mass seemed to be felt.

*Fourth Admission*—Since 1941 when the ileocecalostomy was performed, the patient had had several episodes of intestinal obstruction successfully relieved by the use of the Miller Abbott tube. In the latter part of May, 1942, she developed another such episode which did not respond very well to intubation. Then, fore, she was admitted to the Mount Sinai Hospital June 19, 1942, and discharged Aug. 19, 1942. During this stay she was found to be chronically ill, anemic, dehydrated and showing evidence of marked inanition. With the Miller Abbott tube in place there was no abdominal distention and only slight tenderness in the right lower quadrant. There were three well healed scars on the left abdomen: (1) left colectomy, (2) valvularo-sphincteromy, (3) ileocecalostomy.

On June 20, 1942, operation was carried out through a left lower periumbilical incision. The end of the Miller Abbott tube was found to reach almost to the ileocecal junction, the stoma of which was satisfactory. The cause of the obstruction was seen to be due to the incarceration of a loop of small bowel beneath the free margin of the mesentery of the ileum just proximal to the anastomosis. The obstruction was easily relieved and the free edge of the mesentery was sutured to the posterior patch.

For about two weeks postoperatively the course was smooth with resumption of frequent loose bowel movements. Then the patient again developed nausea, vomiting, of distention, and fever. Further attempts at intubation failed. On the tenth postoperative day the lower angle of the wound was inflamed with progressive suppuration, so that it was necessary to incise and drain the wound one month following this last operation. It was at that time intra-peritoneal suppuration existed as well as that in the wound. Further progress was slow and at the time of discharge from the hospital the wound showed clean granulation, but no evidence of suppuration.

*Fifth Admission*—The patient was at home for ten days when she was again readmitted, Aug. 20, 1942 and discharged, Oct. 21, 1942. On the day before this admission she suffered severe lower abdominal cramps with nausea and persistent vomiting. An enema had been fairly effective. She still appeared chronically ill and poorly nourished. The abdomen was moderately distended. A nontender immobile sausage-shaped mass was palpated in the right lower quadrant. Numerous baricramps were heard. Rectal examination revealed a small amount of stool. Hemoglobin was 40 per cent, white blood cells were 12,200. Urine contained albumin and acetone. Blood culture was sterile. An intravenous infusion was again started and an attempt was made to pass the Miller Abbott tube. The mass in the right lower quadrant became tender and the temperature rose to 102° F. Some sort of pericolic exudate was thought to exist and accordingly sulfathiazole was administered. About one week later the mass was noted in the umbilical region. The fever gradually subsided. Two weeks later, after a few days of intensely severe cramps the patient noted a mass extruding from the rectum. This was a portion of gangrenous bowel which was completely extruded in the next twelve hours. It measured fifteen inches in length. Following this she felt well. In view of the disappearance of the mass from the right lower quadrant and subsequently from the umbilical region, it was concluded that the extruded

extending from the ensiform to a point two inches lateral to the umbilicus. The gall bladder was distended to twice the normal size, adherent to the common bile duct and duodenum, and contained four pigmented stones 3 to 7 mm. in diameter. The common bile duct was explored and a stenosis was found at its lower portion where a probe could be passed into the duodenum with difficulty. Bockus dilators were introduced with gradual dilatation of the stricture and sphincter. A T tube was inserted and the gall bladder was removed. The



Fig 3.—Roentgenogram made with barium enema following evacuation Dec. 6, 1944 about two days following spontaneous extrusion of sloughed ileum. Evidence of colitis persists. Note incomplete filling of cecum due to persistent infolding, contrast outline and position of cecum with that in Figs. 1 and 4.

right lower quadrant was not thoroughly explored because of extensive adhesions and because of the position of the laparotomy incision. However, the mass felt from time to time in the right lower quadrant was palpated intra-abdominally and ascertained to be the cecum or ascending colon or both. Therefore, partial intussusception of these portions of the bowel was presumed still to exist.

Following the cholecystectomy and common duct drainage the patient had a smooth postoperative course. Cholangiogram made two weeks after operation showed the dye to enter the duodenum readily. There was no abnormality in the extrahepatic biliary ducts. The T tube was withdrawn on the seventeenth postoperative day and she was home three weeks after operation.

previously after a prolonged illness. The most recent operative wound had become infected and was drained on several occasions. This resulted in an incisional hernia to the left of the midline in the lower abdomen. Three steel wire sutures had remained and from time to time had penetrated the subcutaneous tissues producing painful hematomas. At operation the scar was excised and the fascia exposed for two inches all around the defect. Three steel sutures were removed and the defect repaired by mattress sutures of chromic catgut without incising or opening the fascia or peritoneum. She vomited considerably for the first few days postoperatively. This was controlled by Levine tube and intravenous infusions. Three weeks following operation the patient was out of bed and eating an unusually large



Fig. 2—Roentgenogram made with barium enema, Oct. 25, 1917, about one month following spontaneous extrusion per anum of infusum-vitum consisting of excluded terminal ileum. Note absence of cecum and ascending colon due to persistent infusum-vitum.

fatty meal, whereupon typical biliary colic developed with fever and subsequent mild jaundice. There were tenderness and moderate rigidity in the right upper quadrant. Leucine index rose to twelve. Cholecystography with double dose of dye repeated on two days failed to visualize the gall bladder.

*Final Admission (Scurvy).* The patient was admitted to the Mount Sinai Hospital Nov. 29, 1913, and discharged Dec. 21, 1913, because of several previous attacks of biliary colic, with fever and jaundice and failure to visualize the gall bladder on cholecystography. At operation the abdomen was entered through an oblique incision seven inches in length

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Fig 3—Roentgenogram made with barium enema following evacuation Dec 8 1944 about two years following spontaneous extrusion of sloughed ileum. Evidence of colitis persists. Note incomplete filling of cecum due to persistent infolding; contrast outline and position of cecum with that in Figs. 1 and 4.

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Fig 2—Roentgenogram made with barium enema Oct. 20, 1942 about one month following spontaneous extrusion per anus of intussusception, consisting of excluded terminal ileum. Note absence of cecum and ascending colon due to persistent intussusception.

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*Final Admission (Seventh).—*The patient was admitted to the Mount Sinai Hospital Nov. 29, 1943, and discharged Dec. 21, 1943, because of several previous attacks of biliary colic, with fever and jaundice and failure to visualize the gall bladder on cholecystography. At operation the abdomen was entered through an oblique incision seven inches in length

*Final Admission (Eighth)*—Because of recurrent attacks of pain in the right lower quadrant of the abdomen, the patient was admitted to the Mount Sinai Hospital Jan. 2, 1946, and was discharged on Jan. 8, 1946. A right retrograde pyelogram revealed the stones in the right kidney pelvis to have increased in size to a slight degree. However, the right kidney pelvis showed no hydronephrosis. Renal function was good. Sigmoidoscopy to the extent of eight inches revealed no abnormality in the rectum or lower sigmoid. A barium enema (Fig. 4) revealed the entire cecum to fill out at this time in contrast to roentgenograms made in 1942 and 1944 (Figs. 2 and 3). There was no longer any evidence of intussusception of the cecum. Moreover, a small defect seen on the medial wall of the cecum near the ileocecal valve was interpreted as the remaining stump of the ileum which had sloughed off in 1942. Since the colon showed no further retrogression of the pre-existing colitis and the infolding of the cecum had been reduced by repeated enemas, no indication for operation (possible colectomy) was present.

#### SUMMARY OF CASE REPORT

The case reported is that of a 45-year-old white woman first seen in 1940 for nonspecific ileocolitis of two years' duration. Immediately following ileosigmoidostomy with division and exclusion of the distal ileum, she developed repeated attacks of small bowel obstruction. For one year these bouts were controlled by the prolonged use of an indwelling Miller-Abbott tube. The longest such period of decompression was three weeks.

Finally, operation disclosed the obstruction to be due to the insinuation of the ileum behind the mesentery of the divided terminal ileum used in the ileosigmoidostomy. An intra-abdominal abscess and wound infection followed this "clean" operation wherein the bowel was neither opened nor unduly manipulated.

Recurrent abdominal pain, distention, and fever were accompanied by a mass in the right lower quadrant, which, later, seemed to move to the umbilical region. All the abdominal symptoms subsided with the passage of a gangrenous segment of bowel which was presumed to be the excluded loop of terminal ileum.

The sequence in which the patient submitted to operation was:

1. Salpingo-oophorectomy followed by menopause, 1925.
2. Left ureterolithotomy, 1934.
3. Ileosigmoidostomy with exclusion, February, 1941.
4. Release of small bowel obstruction due to insinuation of ileum beneath mesentery, June, 1942.
5. Several incisions and drainage for intra-abdominal abscess and wound infection, July and August, 1942.
6. Repair of incisional ventral hernia, September, 1943.
7. Cholecystectomy and common duct drainage, December, 1943.

#### COMMENTS AND CONCLUSIONS

1. The intussusception of the excluded distal loop of ileum is most unusual. It has been reported only once in the literature and on that occasion spontaneous expulsion of the intussusceptum did not occur as in the case herein reported.

2. Garlock's observation of intussusception of the excluded ileum in two cases (unreported) and in the case under discussion indicates that ileocolostomy

*Follow-up Notes.*—March 16, 1944, general condition of the patient was excellent. All scars were well healed. She had five or six bowel movements daily, but suffered no pain or discomfort.

On Dec 7, 1944, she had suffered some pain in the right lower quadrant for a few days. In view of the history and the presence of a mass in the right lower quadrant without symptoms of obstruction, a barium enema was made. This showed the stoma between the ileum and sigmoid to be functioning well. The colon again showed the loss of haustration, the smoothness of outline, and irregularities noted in 1940 and 1942. At this time (Fig 3) the evacuation film disclosed better filling of the ascending colon, but the cecum was not completely filled, indicating persistent infolding of this part of the bowel.



Fig 4.—Roentgenogram made with barium enema Jan 3, 1946, about 1½ years following extrusion of excluded ileum. Note the complete filling of the cecum and the improved appearance of the colon. On the medial aspect of the cecum at the site of the ileocecal valve is seen a small projection which is interpreted to be the remains of the stoma of ileum.

On Jan 4, 1945, the patient felt well except for moderate persistent pain in the right lower quadrant. She had an average of six bowel movements a day. She maintained her weight. All abdominal scars were well healed without hernias. The anastomosis, symptomatic, and economic results were estimated as good.

On July 5, 1945, she continued to have mild pain in the right lower quadrant, but there were no further symptoms of intestinal obstruction.

# INTERMITTENT EXTERNAL BILIARY DRAINAGE FOR RELIEF OF PRURITUS IN CERTAIN CHRONIC DISORDERS OF THE LIVER

RICHARD I. VARCO, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota)

**I**N CERTAIN chronic disorders of either the hepatic parenchyma or intra-hepatic biliary system, intractable itching is an unpleasant feature. The pruritus in these patients has been commonly ascribed in medical textbooks to an abnormal accumulation of serum bile salts. These individuals frequently suffer miserably from this unremitting annoyance, and their generalized cutaneous excoriations attest to the transient or incomplete relief obtained through the therapy customarily employed. DHE (dihydroergotamine), injected intramuscularly, will often control the pruritus for a short while, but is invariably followed with a return of the desire to scratch. Unpleasant side actions, a brevity of alleviation, and failure of the remedy in certain cases have been encountered during therapy with this drug. Intravenous novocain, according to the method of State and Wangenstein,<sup>1</sup> has been tried, but likewise is only temporarily effective. Sundry sedatives, hypnotics, and analgesics are without prolonged benefit, and in certain instances expose the recipient to the hazard of addiction.

If, in these patients, the abnormal retention of bile salts is associated with or is the cause of the pruritus, then relief from the itching may be anticipated if it is possible to reduce this concentration in the circulation. A rational therapeutic approach, therefore, appeared to be the development of some method for the reduction of the serum bile salt level. Reasonable alterations in the diet offered little hope of reducing the serum bile salt concentration, since these people should receive a high protein intake for the therapy of the chronic hepatic disease.<sup>2</sup> Since, however, from the total quantity of bile salts secreted each twenty-four hours, about 90 per cent is reabsorbed from the intestinal tract, recirculated through the liver, and then re-eliminated in the bile, a pre-enteric de-ation of bile should theoretically eventually reduce the serum bile salt level. These conjectures have been translated into surgical procedures applied to clinical material, and it has been found that intermittent external biliary drainage suffices to attain and maintain prompt and virtually complete relief from this type of pruritus.

Seven operations have been performed on six patients without fatality. In one, cholecystostomy proved unsatisfactory, for after a week or two of post-operative relief from the pruritus, this symptom recurred when the drainage decreased virtually to zero. Three patients had a cholecystostomy and catheterization of the common bile duct via the cystic duct. In these cases there has been some difficulty in reinserting a catheter through this opening when it became necessary to replace this tube about six to eight weeks after surgery. Cholecystostomy and drainage of the common bile duct with a T tube has been the operative procedure three times. This plan has been consistently effective; however, since the common bile duct is undilated in this type of case,

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with exclusion cures the disease in the terminal ileum. Intussusception can hardly be expected to develop in the ileum unless it were sufficiently distended.

3. Intestinal obstruction following operations for colitis is known to be rather common. Usually it is due to postoperative bands or adhesions. However, the cause of the obstruction may be varied. In this case it proved to be due to (1) insinuation of the ileum behind the divided mesentery near the stoma, (2) wound infection, and (3) intussusception of the excluded ileum.

4. In performing ileocolostomy with exclusion both the divided mesentery and the terminal ileum should be tacked down to prevent the two complications observed in this case.

5. This case represents a triumph for the several surgeons who contributed to the treatment of a woman who, although she appeared neurotic, invariably developed definite evidence of organic disease.

6. In spite of seven major operations and at least twelve hospital admissions during which she was frequently close to death, she finally achieved a stable well-being.

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control of 0.71 mg. per cent. Clinically, the relief from pruritus was virtually complete, and to the patient, wholly satisfactory. Unfortunately, the choledochostomy catheter became untethered while she was home and was not replaced for so long an interval that the fistula closed over. Within a few weeks the itching had returned in such intensity that she requested operative relief. On Feb. 14, 1946, a T tube was placed in the common duct and with the development again of external biliary drainage, the itching urge was controlled. Convalescence from both procedures was without event, and the patient has remained well and free from distress in opening the external limb of the T tube for a few hours daily. The consistent decline in the bile salt content (Table II) of the bile drainage, analyzed daily postoperatively, supports the thesis of an enterohepatic circulation, for with the external shunt permitting less bile salts to enter the intestine diurnally, but following day's value is consecutively reduced.

#### DISCUSSION

Small quantities of bile salts have been given orally upon three occasions to patients in this series during the time each had an external biliary fistula. Pruritus promptly returned and then disappeared with maintenance of the external biliary drainage.

In no instance has it proved necessary to develop a complete or even high grade deviation of the bile in order to provide satisfactory surcease from the itching. Circuiting the bile to the outside for short intervals daily has sufficed to keep these persons comfortable. In all patients, chronic hepatic disease has been the preoperative diagnosis, and this has been confirmed by the pathologic report of liver biopsies secured during the surgical procedure. It should be emphasized that pruritus associated with acute hepatitis is so frequently a self-limited disease, that any surgical procedure for its relief would seem unwarranted.

The elevation of the serum bile salt level in these patients with chronic hepatic disease has been quite independent of any relationship, direct or reciprocal, to pigment retention. Jaundice therefore cannot be quantitatively assayed but is then interpreted as a reflection of the need for this procedure. Indeed, many of the patients studied have had virtually no bilirubinemia. Jaundice per se, so convincingly demonstrated in these instances of hemolytic anemia, cannot evoke pruritus. This differential retention of bile salts in the serum exemplifies another instance of one altered hepatic function with many others remaining seemingly unimpaired.

#### SUMMARY

Intermittent external biliary drainage has been employed with success for the relief of pruritus occurring in certain patients with chronic hepatitis or cirrhosis.

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a rather small caliber T tube, size 10 or 12 French, must be available, and may pose some minor technical difficulty.

All analyses for bile salt content were carried out according to the method of Josephson<sup>4</sup> for blood, and Reinhold and Wilson<sup>5</sup> for bile.

Table I presents data relative to the blood levels preoperatively, and then the reduction in these values following a postoperative period of external biliary drainage. In Table II, the blood level for bile salts is charted pre- and postoperatively. A reduction can be noted following the phase of external biliary drainage. During the period of this study there is also demonstrated a definite downward trend in the percentage of bile salt in the biliary secretions, as one would predict after interposing a shunt into the enterohepatic circulation of this component.

TABLE I BILE ACIDS CONCENTRATION

IN BLOOD						IN BILE			
PREOPERATIVE (MG. %)			POSTOPERATIVE (MG. %)			OPERATIVE		POSTOPERATIVE	
DATE	PA	CON.	DATE	PA	CON.	DATE	MG. %	DATE	MG. %
11/11/45	4.45	0.2	2/14/46	2.70	0.45	2/4/46	18.5	2/14/46	7.5
A.R.	4.27	1.50	11/5/45	0.65	0.71				

TABLE II LEVEL FOR BILE SALTS IN PATIENT A. R. CHARTED PREOPERATIVELY AND POSTOPERATIVELY

BILE ACIDS CONCENTRATION IN BLOOD				
DATE	VOLUME (CC)	BILE ACIDS CONCENTRATION IN BILE (MG. %)	PATIENT (MG. %)	CON. BILE (MG. %)
2/4/46			1.17	0.50
2/15/46	215	12.50	(Preoperative)	
2/16/46	468	15.98		
2/17/46	480	12.00		
2/18/46	445	9.00		
2/19/46			0.45	0.45
2/20/46	625	7.50	(Postoperative)	
	565	4.50		

## CASE REPORT

A. R. (U. H. No. 75372) was first admitted May 15, 1945. She had been bothered persistently for eight years by generalized pruritus of varying intensity. Through the years her skin had thickened and become darker, but so far as she knew, it never been visibly jaundiced. These facts were confirmed in a physical examination, which revealed an enlarged, slightly tender liver but was otherwise essentially noncontributory. Liver function studies suggested definite hepatic damage. Thirty per cent of bromsulphalein (5 mg. per kilo) was retained at forty five minutes. An hyperurubinogenemia was present upon repeated examinations. The prothrombin time, twice the control returned to normal after 64 mg. of vitamin K parenterally. The serum bilirubin was 1.0 mg. per cent at 1 minute with a total of 1.9 mg. per cent. Peritoneoscopy at this time indicated the characteristically hobnailled liver of Laënnec's cirrhosis. A rather severe reaction followed this procedure, but the patient was eventually discharged and advised to consider submitting to an operative procedure for the control of her pruritus. She returned and a cholecystostomy and catheter choledochostomy via the cystic duct was carried out Oct. 9, 1945. The enlarged, nodularly fibrotic liver was biopsied and microscopically identified as cirrhotic. Her serum bile salt level declined from a preoperative value of 3.2 mg. per cent with a control of 1.2 mg. per cent to a postoperative value of 0.65 mg. per cent and a

2. A most popular conception is that the spleen destroys effete blood cells of the circulation, yet there is no potent evidence to uphold this view. Blood drawn from the splenic artery and vein fails to show any difference in the urobilinogen content, which would be the case if active destruction took place in the spleen. If the red cells were destroyed in the spleen, there would be an increase in the iron content as revealed by special stains. This has not been shown to be the case. Phagocytosis of the red and white cells by the reticulo-endothelial cells has been demonstrated, but only to a minor degree, and not sufficiently to make this a great function of the spleen. It is thought that excessive destruction of platelets by the spleen is the responsible factor in thrombocytopenic purpura, but no definite evidence of this has been found in the spleens removed from patients with this disease. In congenital hemolytic anemia the fragility of the red blood cells is increased and spherocytosis appears. While most patients become completely asymptomatic following splenectomy, increased fragility and spherocytosis usually persist.

3. The great vascularity of the spleen is well known. By virtue of its rhythmic contractions it regulates the blood flow to the gastrointestinal tract during digestion. In extreme oxygen want, as seen in severe anemia, at high altitudes, and in carbon-monoxide poisoning, the spleen pours out into the circulation its large reserve of red cells.

4. According to Naegeli, the spleen in some unknown way possesses hormonal action. He suggested that some substance is liberated by the spleen which has a hemming action on the bone marrow. Removal of the spleen permits overactivity of the bone marrow and an outpouring of immature red and white cells and platelets into the peripheral circulation. This may be the mechanism for improvement following splenectomy in congenital hemolytic anemia, thrombocytopenic purpura, Doan's neutropenia, and even splenic anemia. This is further evidenced by the fact that histologic examination of the spleen throws no light on the local mechanism as an etiologic factor.

#### CONGENITAL HEMOLYTIC JAUNDICE

Congenital hemolytic anemia is characterized by the following: (a) A severe anemia, jaundice, and microspherocytosis. Reticulocytes are increased in number and nucleated red blood cells are often found in the peripheral circulation. There is usually a leucocytosis. (b) The fragility test is the most important laboratory procedure in this disease. Normally, hemolysis of red blood cells begins in a salt concentration of 0.42. In congenital hemolytic jaundice the hemolysis begins at higher concentrations. (c) The icterus index is elevated and the van den Bergh test gives an indirect reaction. (d) There is an increased amount of urobilinogen in the urine and no bilirubin present, hence the term "acholic jaundice." (e) Bone marrow studies usually reveal a preponderance of the erythroid series over the myeloid. The only abnormal type of cell present is the spherocyte.

Following splenectomy in this disease, the preoperative fragility index does not change and spherocytes may still be found in the peripheral blood. Gallstones of the calcium bilirubinate type may be found in 30 to 40 per cent



## SPLENECTOMY

### AN ANALYSIS OF THIRTY-EIGHT CASES

JEROME F. TANNA, M.D., NEW ORLEANS, LA.

(From the Charity Hospital)

AT THE Charity Hospital, New Orleans, La., during the period from Jan. 1, 1939 through 1945, there were thirty-eight splenectomies performed. This number does not include those done for trauma, neither does it include those done during the course of esophagectomy or total gastrectomy. Eleven of these splenectomies were done for congenital hemolytic anemia, one for acquired hemolytic anemia, four for idiopathic thrombocytopenic purpura, ten for Banti's syndrome, one for splenic neutropenia, six for sickle cell anemia, one for splenic torsion, one for aleucemic leucemia, and three for "unknown etiology." For various reasons, splenectomy was not done on all patients with a final diagnosis of the various conditions mentioned here. For instance, during this period there were thirty-seven patients with a final diagnosis of congenital hemolytic anemia, forty-two of acquired hemolytic anemia, twenty-four with idiopathic thrombocytopenic purpura, seventy-seven with Banti's syndrome, three with splenic neutropenia, two hundred sixty-seven with sickle-cell anemia, two with splenic torsion, and fifteen with aleucemic leucemia.

The relative rarity of these diseases is recognized when one realizes that during this time period there was a total of 361,382 admissions.

The operation of splenectomy is said to enjoy considerable antiquity. Rational splenectomy, apart from that predicated by acute surgical conditions, especially traumatic cases, was not established by empirical experiment until the early part of the twentieth century. The pioneer work of Barciofi, McNee, Lord Dawson, and Krumphaar in creating sound fundamental ideas of physiologic splenic functions has been supplemented by the controlled studies of pathologic splenic diseases by the hematologists Kaznelson, Frank, Dameshek, Doan, Wiseman, and others.

### FUNCTIONS OF THE SPLEEN

1 The spleen as an hemopoietic organ. In the embryo, the spleen, along with the liver, assumes the chief role of the formation of blood cells. After birth, this function is taken over by the red bone marrow. In certain disease states involving the hematopoietic system of the adult, the spleen is capable of resuming its embryologic function. In adults, the spleen normally supplies lymphocytes and monocytes to the circulation. The large reticuloendothelial cells of the spleen are thought by some to play a role in the metabolism of fat, especially cholesterol. The reticuloendothelial cells also play a role in the production of antibodies for the body.

good results from splenectomy. Examination of one of these patients two years after operation revealed that he had gained weight and that he was no longer anemic. The other patient, examined approximately two years after operation, showed a marked improvement in his anemia, the red blood cell count having risen to 4,450,000 from a preoperative count of 960,000.

Four patients showed no improvement whatsoever over their preoperative status.

Four patients died; one, two weeks after operation, with postmortem examination revealing retroperitoneal reticulum cell sarcoma; another, one year after operation, from gastrointestinal hemorrhage; the third, the same day of operation, as the result of a slipped splenic pedicle; and the cause of death was not indicated on the chart of the fourth patient.

It is possible that the two patients in this series classified as showing improvement following splenectomy may fall in that group of patients described by Blakemore and Lord as being amenable to splenectomy alone.

#### DOAN'S NEUTROPENIA

Wiseman and Doan,\* in 1942, following a preliminary report in 1939, introduced a newly recognized syndrome characterized by marked neutropenia and splenomegaly. They feel that this syndrome is comparable to congenital hemolytic icterus and thrombocytopenic purpura. In congenital hemolytic icterus there occurs excessive erythrocyte destruction, in thrombocytopenic purpura an excessive platelet destruction, while in splenic neutropenia there exists an excessive destruction of white blood cells. It is most interesting that the selective action of the elastomocyte of the spleen is capable of producing three distinct clinical entities.

The salient diagnostic features are splenomegaly, purpura (depending on the degree of associated thrombocytopenia), oral ulceration (depending upon the acuteness and severity of the neutropenia), and, occasionally, mild icterus (depending on the degree of associated hemolytic anemia).

The bone marrow shows hyperplasia of the myeloid series and, if hemolytic anemia is pronounced, of the erythroid series. The marrow is not leucemic and no abnormal cells are present.

The blood shows marked specific neutropenia. If anemia is present, it is macrocytic and hyperchromic in type. If anemia is definite, reticulocytosis is present, and there is an increased, indirect, van den Bergh reaction. The thrombocytopenia is variable.

Experience, so far, shows that splenectomy is specific therapy for this disease in that the patients are restored to a normal hemopoietic equilibrium.

One splenectomy in this series was done for splenic neutropenia. The subject was a 23-year-old, white man with splenomegaly, leucopenia, hemolytic anemia, and thrombocytopenia. The bone marrow was hyperplastic for the granulocytic series and the patient had ulcers of both legs. The preoperative laboratory findings were: red blood cells, 3,900,000; white blood cells, 1,100; polymorphonuclears, 61 per cent; platelets, 100,000. The laboratory follow-up one and one-half years following splenectomy showed decided improvement.

phase, with splenomegaly, asthenia, and occasional hemorrhage; (2) the transitional stage, with oliguria, urobilinuria, hepatomegaly, brown discoloration of the skin, and increasing gastrointestinal bleeding; and (3) an ascitic stage, with atrophy of the liver, subicteric sclerae, hemorrhage from the mucous membranes, and death from hemorrhage or liver insufficiency.<sup>6</sup>

According to Blakemore and Lord,<sup>7</sup> it is necessary to determine the site of portal obstruction before rational therapy can be instituted. One can predict, on the basis of liver function chemistry, whether the portal hypertension is due to intrahepatic (portal cirrhosis), or extrahepatic portal bed block. If the liver is the site of the portal block, i.e., portal cirrhosis as manifested by deficient liver function, splenectomy alone will not effect a cure. In this type of case it is necessary to perform a portocaval shunt in addition to the splenectomy. They describe in detail their technique, using the vitalium tube, non-suture method of anastomosis between the portal and caval systems.

Even when the block is extrahepatic but proximal to the entrance of the coronary vein into the portal system, splenectomy alone will not effect a cure. It is only in those cases in which the obstruction is distal to the entrance of the coronary vein, into the splenic vein that splenectomy alone will give a satisfactory result with relief of hematemesis, anemia, leucopenia, and thrombocytopenia.

These authors use manometric readings made at various points of the portal system to determine the site of obstruction. For example, in a patient with congestive splenomegaly in which the superior mesenteric pressure is normal, the splenic vein pressure elevated, but the coronary vein pressure approximately normal, splenectomy only would be indicated. A normal reading from the superior mesenteric vein and an elevated reading from a branch of the coronary vein would make mandatory splenorenal anastomosis following splenectomy.

It is hoped that these recent concepts of Banti's disease might alter the poor results that have been obtained in the past.

In a discussion of Banti's disease it is interesting to call attention to the Cruveilhier-Baumgarten syndrome. Bruno<sup>8</sup> states that, up to 1947, sixty-six patients with this condition have been reported in the literature. This syndrome is characterized by the clinical picture of portal hypertension, evidence of excessive umbilical circulation, and the presence of a loud abdominal murmur and thrill. The murmur and thrill are due to the rich anastomosis between umbilical or para umbilical veins and the thoracoabdominal veins in attempting to establish a collateral circulation.

Of the ten patients on whom splenectomies were done following diagnosis of Banti's disease, six were white and four were colored; seven were male and three female; and the ages ranged from 8 to 64 years. The findings were variable. All suffered with anemia which was secondary to bleeding hemorrhoids, esophageal varices, or lower gastrointestinal pathology, possibly purpuric in character: the spleen was enlarged in all patients, the liver was mentioned as having been enlarged in five, and ascites was listed in three.

The pathologist's report of the removed specimens was "uniformly splenic fibrosis and congestion." Two patients may be classified as obtaining fairly

in the left, upper, abdominal quadrant, red blood cells, 4,000,000; white blood cells, 10,350; lymphocytes, 82 per cent.

Splenectomy was done without any idea of what the diagnosis was, but with the hope that removal of this "mass" might help the patient. Two months following splenectomy, the patient returned for a check-up and stated that he actually felt better, having been relieved of the dyspnea and the heaviness in the upper abdomen. There is no further follow-up on this patient. The pathologist's report was "lymphatic leucemia."

I feel certain that, had the diagnosis been known before operation, splenectomy would have never been done. There is complete agreement that splenectomy is of no value in the leucemias.

#### UNKNOWN ETIOLOGY

There were three patients in the series that had splenectomy and on whom a final diagnosis could not be made.

One patient, a white woman, age 52, came into the hospital complaining of epigastric burning and abdominal distention. X-ray revealed a calcified body in the left, upper, abdominal quadrant. Exploration was done for the possibility of a calcified spleen and partial intestinal obstruction. In the operative note it was mentioned that the spleen was enlarged and removed. The report of the pathologist revealed spleen engorged with red blood cells. The patient was discharged still complaining of epigastric burning. The chart showed no further follow-up of the patient.

The second patient, a white woman, aged 56, was admitted with pain in the back, tenderness, and pain in the left, upper quadrant. The spleen was enlarged and splenectomy was done under a preoperative diagnosis of splenectomy of unknown etiology. At operation, calcification of the splenic artery was noted, the spleen was twice the normal size, and several calcified lymph nodes were found in the hilum. The pathologist's report was "splenic fibrosis." The patient was discharged free from pain, and no further follow-up was recorded on the chart.

The last patient, a white woman, age 38, had splenectomy because of pain in the abdomen and legs and a mass in the left, upper quadrant. At operation the spleen was of normal size and there were no areas of calcification noted. The pathologist's report was "chronic splenitis." The patient was discharged unimproved.

It seems that, in the last three cases, splenectomy was done for want of something better to do. It is doubtful that any of the patients ultimately noticed any relief.

#### OTHER INDICATIONS FOR SPLENECTOMY

Surveying the literature, one finds reported instances of splenectomy with apparently good results for various splenopathic states.

According to Paul,<sup>12</sup> cysts of the spleen are very rare. He classifies cysts of the spleen as follows:

I. Hydatid cysts

II. Cysts associated with polycystic disease of the kidneys

red blood cells, 5,100,000; white blood cells, 8,520; polymorphonuclears, 55 per cent; and platelets, 219,600. The general condition of the patient was also markedly improved.

#### SICKLE-CELL ANEMIA

Sickle-cell anemia occurs only in Negroes. Women are affected more than men. Five to ten per cent of all Negroes possess sickling trait, but only 10 per cent showing a sickleemia develop an associated anemia.

The findings are: weakness, fatigue, anorexia, abdominal pain, icterus of sclerae, and pain in left upper quadrant from splenic infarcts. Arthritic manifestations and ulcers of the leg are not uncommon. Shortly after a crisis, examination reveals an icteric tinge to the sclerae, pallor of mucous membranes, enlargement of the liver and spleen, enlargement of the heart with hemic murmurs, tenderness and spasticity of the abdominal muscles, elevated temperature, and increased pulse and respiratory rate. Between crises, symptoms are mild and there may be no splenic enlargement.

Examination of the blood reveals the characteristic sickling of the red blood cells, leucocytosis, and erythroblastic activity. In the chronic form in children, the bones show a thickened marrow space with thinning of the cortex.

The value of splenectomy in this condition is doubted by most authorities because lymph nodes and other reticuloendothelial tissue may carry on the phagocytic function of the spleen even if it is conceded that the spleen is responsible for deterioration of the red blood cells.<sup>10</sup>

The pediatric and surgical units at Charity Hospital agreed to try splenectomy on some of these patients to determine what could be accomplished. Follow-up statistics over a two-year period on the six patients treated by splenectomy in this series show that the results are anything but encouraging.

All of these patients were of the colored race, and four were male. The ages varied from 22 months to 7 years.

#### TORSION OF THE SPLEEN

Sheppard,<sup>11</sup> in 1944, made note that there were twenty-five recorded cases of splenic torsion. He reported upon one of his own patients splenectomized with a successful outcome.

Abdominal pain, vomiting, signs of shock, adynamic ileus, and signs of peritonitis have been outstanding features of this condition. The clinical picture may closely resemble intestinal obstruction.

In the present series there was one patient. This patient was a white woman, 24 years old. On admission, she presented severe pain, vomiting, and a large, tender mass in the abdomen. A preoperative diagnosis of twisted ovarian cyst was made. At operation, the spleen was found to be enlarged and twisted three times upon itself. Splenectomy was done, and the patient made a remarkable recovery. The pathologist reported thrombosis of hilar vessels with massive splenic infarction.

#### ALFUCIMIC LIUCENIA

A colored man, age 66, was admitted with the following findings: loss of weight; enlargement of the abdomen, shortness of breath; a hard mass palpable

lant's disease, the cases should be evaluated very carefully as recommended by Whipple, and Blakemore, and Lord.<sup>4, 5</sup>

3 Splenectomy was found to be of little or no value in the patients with sickle-cell anemia, aleuemic leucemia, and those splenectomized under the diagnosis of "splenomegaly of unknown origin."

4 Other conditions for which splenectomy has been done with good results are discussed.

5 Some of the contraindications are discussed.

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### III. Single cysts:

(a) dermoid

(b) epidermoid

(c) serous and blood cysts, devoid of epithelial lining

### IV. Multiple serous cysts.

The symptoms in most of these patients are attributable to pressure. The treatment of choice is splenectomy.

Hausmann and Gaarde<sup>13</sup> report one case of splenectomy for reticulum cell sarcoma. The patient ultimately expired because of recurrence. Malignancies of the spleen may be classified as follows. (1) fibrosarcoma; (2) endothelioma; (3) lymphosarcoma and Hodgkin's granuloma; and (4) reticuloendothelial sarcoma. The authors feel that splenectomy is justified if, at exploratory laparotomy, the spleen is the sole focus of the pathologic process. They mention that patients are alive at the end of four to eight years.

Steinberg<sup>14</sup> advises splenectomy for Felty's syndrome after conservative measures have failed. This condition was first described by Felty in 1924. It is characterized by atrophic arthritis, fever, secondary anemia, leucopenia, splenomegaly, and tachycardia. Splenectomy is deemed rational because the bone marrow shows hyperplasia and it is believed, therefore, that the spleen stands in the way of blood elements being present in adequate quantities in the blood stream.

### SOME CONTRAINDICATIONS

Reich and Rumsey<sup>15</sup> caution against splenectomy in a condition they term "agranulocytic myeloid metaplasia of the spleen." This condition is characterized by splenic enlargement and the presence of immature red and white blood cells in the blood. It is often erroneously diagnosed as chronic myelogenous leukemia, splenic anemia, erythroblastosis, or Hodgkin's disease. Frequently, the picture is so confusing that a splenectomy is performed with unfavorable results.

In this condition, myeloid metaplasia of the spleen is present and the authors present five cases which show that depression of this focus of myeloid metaplasia by splenectomy definitely places the patient on a downhill course.

This condition is most easily confused with Banti's disease and atypical leukemia. However, Banti's disease does not show both immature red and white blood cells in the peripheral blood, and sternal puncture will rule out leukemia, if no leucemic infiltration is observed in the marrow of the patients.

Carpenter,<sup>16</sup> in his article, concludes that splenectomy is absolutely contraindicated for Cooley's disease and polycythemia rubra vera.

### SUMMARY AND CONCLUSIONS

1. An analysis of thirty-eight splenectomies done at the Charity Hospital, New Orleans, La., during the period from Jan. 1, 1939 through 1945, is presented.

2. It can be concluded that splenectomy is definitely indicated for congenital hemolytic anemia, idiopathic thrombocytopenic purpura, splenic neutropenia, and splenic torsion. Before splenectomy is done in cases of so-called

Banti's disease, the cases should be evaluated very carefully as recommended by Whipple, and Blakemore, and Lord.<sup>6,7</sup>

3. Splenectomy was found to be of little or no value in the patients with sickle-cell anemia, aleuemic leukemia, and those splenectomized under the diagnosis of "splenomegaly of unknown origin."

4 Other conditions for which splenectomy has been done with good results are discussed

5. Some of the contraindications are discussed

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On the second postoperative day the hemoglobinemias had disappeared and the plasma was straw colored, but the urea nitrogen was 70 and the urine output, with an intake of 2,230, was 440 c.c. Five per cent sodium bicarbonate was again given, and was followed by 500 c.c. of matched, citrated whole blood (the first transfusion).

The oliguria continued, and fluids were administered conservatively. By June 4 urea nitrogen was 109, the creatinin was 5.2, the CO<sub>2</sub> was 53, and the plasma proteins were 5.8. He had continued apathetic and had developed moderate generalized edema; the blood pressure was 190/102. Peritoneal lavage as described by Fino and associates was instituted on June 5, and transfusion was given a second time with citrated blood, preceded by 5 per cent sodium bicarbonate. Penicillin was given intramuscularly and streptomycin was added to the lavage fluid. Auricular fibrillation appeared and digitalization was done by another doctor. By June 9, the urea nitrogen had fallen to 67 mg. per cent, and the edema had diminished, possibly because 5 per cent glucose had been added to the fluid used to lavage the peritoneum (see Table I). However, he died, apparently from pulmonary edema, on June 9. The maximum urian output in any one twenty four hour period after operation never exceeded 825 c.c.

TABLE I. FLUIDS AND METABOLITES

OPERATION	MAY					JUNE							
	28	29	30	31	1	2	3	4	5	6	7	8	9
Fluid intake (c.c.)	2,000	2,000	2,250	3,543	2,220	1,010	2,550	2,150	1,550	1,500	0	85	
Fluid output (c.c.)	550	825	440	600	530	330	500	470	500	450	500	400	
Blood urea N <sub>i</sub>	21	49	79	66	74	62		109		91	87	77	6
Peritoneal lavage													
Input (c.c.)									8,250*	22,700*	23,800†	23,200†	14,100
Output (c.c.)									6,900	23,100	25,100	24,350	14,700
Urea N <sub>i</sub> (grams)									2.3		10.5 <sup>11</sup>		
Total N <sub>i</sub> (grams)										24.3		73.8	

\*Hartmann's solution.

†Five per cent glucose added

Autopsy was performed shortly after death by the pathologist at St. Barnabas Hospital. Nutrition was found to be good. The scrotum and ankles were edematous. There were surgical wounds 6 cm. long in each lower abdominal quadrant. The sclerae were icteric. There was a liter of cloudy fluid, containing flecks of fibrin, in the peritoneal cavity. The peritoneal surfaces were clean.

The left pleural cavity was obliterated by old adhesions, and the right contained 1,500 c.c. of clear, straw-colored fluid. There was mild coronary sclerosis, with cardiac hypertrophy and dilatation. The lungs exhibited basal atelectasis as well as moderate edema and emphysema.

The liver weighed 2,075 Gm. and the cut surface was a mottled reddish brown. The gall bladder was thin walled but contained many stones. The bile ducts were patent. The gastrointestinal tract, pancreas, and adrenals appeared normal.

The kidneys were enlarged (215 and 235 Gm.) but of normal consistency. Both cortex and medulla were thick, and the markings were distinct. The cut surfaces were dark red and homogeneous. The pelvis and ureters were not dilated.

The bladder and prostatic cavity showed the effects of the recent operation. The prostatic capsule had been perforated on the right posterior wall, but there was no extravasation nor periprostatis.

The central nervous system was not examined.



FIG 1.—A, R. K. Section of kidney from autopsy (hematoxylin and eosin,  $\times 100$ ). B, Renal biopsy seventy-two hours after transfusion with incompatible blood (benzidine stain,  $\times 100$ ).

*Microscopic Examination.*—In the lungs the alveoli were distended and contained a moderate number of red and mononuclear cells. The liver showed slight atrophy of central cord cells. In the prostate there was necrosis of cut surface with acute exudative inflammation. There were partially organized thrombi in larger veins. The myocardium had some fragmentation of muscle bundles and separation of fibers. In the kidneys (Fig. 1) pigmented casts filled the

collecting tubules. The epithelium of the convoluted tubules was flattened and their lumina were dilated. The interstitial tissues were infiltrated by lymphocytes and plasma cells. There was mild subintimal hyalinization of the arterioles, and the glomeruli were normal.

*Conclusions*—Conclusions by the pathologist were recent transurethral prostatic resection, postoperative hemoglobinemia, obstruction of the renal tubules by hemoglobin casts, chronic pyelonephritis, uremia (terminal), hypertrophy and dilatation of the heart from hypertension, pulmonary edema, right hydrothorax, chronic passive congestion of the liver, cholelithiasis, and ascites (from peritoneal lavage).

#### BRIEF REVIEW OF THE LITERATURE

It has been known for a long time that transfusions of incompatible blood may produce hemoglobinemia, hemoglobinuria, and renal insufficiency with oliguria or anuria. According to Flink, Denys in 1867 was the first to describe hemoglobinuria after the transfusion of incompatible (heterologous) blood in sheep. The renal changes which result from hemoglobinemia and hemoglobinuria are well known. They have been described in blackwater fever by Barratt and Yorke and by de Haan, after severe burns by Shen, Ham, and Fleming; after crush injuries (myoglobin rather than hemoglobin) by Bywaters and Beall, after obstetrical mishaps associated with infiltration of the uterine muscle with blood by Paxson, Gohli, and Hunter, and after the transfusion of incompatible blood by many investigators.

The renal lesions in these conditions include vacuolation, necrosis, and desquamation of epithelium in Henle's loops and the distal convoluted tubules; pigmented casts are found in Henle's loops and in the convoluted and collecting tubules, and hemosiderin granules are seen in the convoluted tubules. There has been controversy over the nature of the pigmented casts, which have been called hemoglobin, methemoglobin, and acid hematin, but Flink stated that their composition is as yet unknown. They contain no iron, but give a positive benzidine reaction. There has also been disagreement over the exact cause of the renal insufficiency which accompanies the more severe lesions. Baker and Dodds and others have thought that the pigmented casts obstructed the nephron, a view which has been widely accepted and which is supported by the findings in our case; others, however, believe that the hemoglobin or some product thereof damages the renal tubules, and that the pigmented casts are shed by the tubular cells as the result of the action of a toxic agent, plugging being unimportant.

It has been shown experimentally that similar changes in the kidney follow the intravenous injection of solutions of hemoglobin (Levy), and laked red blood cells (Barratt and Yorke); the latter found that the renal lesions were less severe if the stroma of the red cells were filtered out first. The arrival of the hemoglobin in the kidney evidently produces a vasoconstriction since definite shrinkage of the organ has been detected immediately after intravenous injection of laked red cells in the dog by Levy, and of hemoglobin solutions in the frog by Mason and Mann, and in the dog by Hesse and Pilatov. This may be of some importance in renal insufficiency after transurethral



production of renal hypoxia, by the effect of the operation, or more probably by all these. It was a secondary evidence that some damage to the renal tubules can be produced by the intraoperative injection of a solution of hemoglobin, and by lacerated blood, so that they also occur in other forms of hemorrhagic shock, severe trauma, and crush injuries, although in the last instance the toxic factor appears to be myoglobin. If hemoglobinemia alone is to damage the previously normal kidney, it must be very severe.

#### CLINICAL APPLICATIONS TO TRANSURETHRAL PROSTATIC RESECTION

It is customary to use sterile tap or distilled water as the irrigating fluid in transurethral resection. During the course of the operation, especially if it is reasonably complete, many good sized veins may be opened. The resulting hemorrhage necessitates running the water in at a rapid rate (hence under some pressure) in order to wash the blood away from the operative field sufficiently to permit the operator to see what he is doing. It is, therefore, easy to understand how the water, probably by now containing blood already hemolyzed in the bladder, may enter the venous system and there produce hemolysis. It seems possible that several effects may then be expected. First, some vasoconstriction in the kidney probably occurs. If bleeding has already produced or subsequently produces spasm of the renal vessels, some damage to the kidney may be anticipated from a combination of these two factors. If the amount of free hemoglobin is small, it will be excreted in the urine where it escapes attention because of the usual postoperative bleeding. If the amount of free hemoglobin is considerable (it is too soon to speak in terms of actual concentration in the plasma in our clinical cases), plugging of the tubules and toxic changes in their epithelium will then occur.

On the basis of our experience so far, it seems unlikely that hemoglobinemia is often of sufficient severity in transurethral resection to damage the kidney irreparably, but rather that it is one important factor in producing such damage. Other factors which may combine with it include bacteremia, 2, with resultant pyelonephritis, and renal vascular spasm from hemorrhage and from hypotension.

Link and others have seen signs of regeneration in the tubular epithelium in from five to seven days after the onset of hemoglobinemia. If the patient can be kept alive sufficiently long, it is reasonable to assume that recovery may occur even in the presence of an initially severe renal lesion.

#### TREATMENT

Keeping the patient alive with kidneys severely damaged as the result of hemoglobinuria taxes clinical judgment. One must strive to maintain fluid balance without overloading the circulation to the point of pulmonary edema. Oxygen therapy seems indicated in the initial stages, since vasospasm probably damages the tubules by reducing their supply of oxygen (Macintosh, Harvard, and Parsons). Whether the use of the tent or mask can increase the oxygen saturation of the blood sufficiently to be of assistance is very doubtful.

but increasing the supply of oxygen available to the lungs can do no harm. It is possible that the intravenous administration of oxygen might be more helpful.

The intravenous administration of isotonic sodium sulfate has been advised by Neeheles, Kroll, and Olson on the basis of their experience with dogs rendered anuric by experimental burns (shown by Shen, Ham, and Fleming and by others to be due to hemoglobinemia) where its use has been followed by diuresis in each case, but we have not tried it.

The acidosis which usually accompanies uremia must be controlled by the administration of alkalis without overloading the patient with sodium. The inevitable anorexia may require tube feeding and the administration of parenteral vitamins. In the early stages nasal suction may be needed for persistent nausea and vomiting. Proteins may require parenteral replacement, and the anemia resulting from blood loss and hemolysis may demand transfusion. Since a hemolytic reaction has already occurred, matching of the blood should be painstaking. Flink is of the opinion that measures to insure diuresis at the very beginning of the reaction, before oliguria has occurred, may help by diluting and promoting the excretion of the hemoglobin, but the forcing of fluids after oliguria has developed probably is responsible for many fatalities, as it apparently was in this case.

While waste products are piling up in the blood as a result of the oliguria or anuria, one may perhaps gain time for repair of the renal damage and may lessen the toxemia attendant upon the uremia by employing peritoneal lavage. A subject recently reviewed by Fine, Frank, and Seligman. We have had experience with this procedure in but two cases, the other a severe reaction from a transfusion of incompatible blood, and cannot yet evaluate it, but it reduced the urea nitrogen of the blood by 40 mg. per cent in four days in the case under discussion, and autopsy did not show evidence of any serious reaction in the peritoneum. In the second case, however, the lavage, after removing large quantities of nitrogenous substances from the blood, became ineffective after three days because of "waling off" around the inflow and outflow tubes, although it undoubtedly contributed greatly to the patient's recovery. Whether peritoneal reaction can be prevented by changes in the composition of the irrigating fluid (Hartmann's solution with 5 per cent glucose added), or whether it is due primarily to bacterial action, remains to be determined. It can be seen that, even with these limitations, peritoneal lavage may turn the tide in the patient's favor in some circumstances.

It is obvious, however, that the solution to the problem lies in the prevention of hemolysis during transurethral resection rather than in the treatment of the ensuing hemoglobinuria and its effects. One move in this direction consists in using the irrigating fluid at the lowest possible pressure, but the possibility of seeing clearly is unlikely with a pressure low enough to prevent the entrance of fluid into the circulation.

Another possibility is to employ an irrigating fluid which does not hemolyze blood. Saline solution cannot be used because, being a good conductor

of electricity, it diffuses the current from the electrode in the resectoscope enough to prevent satisfactory cutting and coagulating.

Five per cent glucose apparently does not cause hemolysis and so was tried, after this patient had died, at the instigation of Ebert, who had used it for some time for quite another reason. It has been used thus far in about twenty-five cases, and does not appear to interfere seriously with operation, although it does possess certain disadvantages. Postoperative determinations of free hemoglobin in the plasma have been made in every case and have shown measurable amounts in some instances (an effect of burning of tissue by surgical diathermy<sup>9</sup>), but no disturbingly high levels have yet been found.

Since blood is not hemolyzed, brisk bleeding interferes, with vision more than it does when water is used because the medium is hazy, but this would be true of any nonhemolytic fluid, and so far has not been very troublesome.

Gloves become somewhat sticky as the glucose solution dries on them, but it is easily washed off.

Determination of the loss of blood by the method of Conger and Nesbit cannot be made without some modification of that method. Apparently if plain water is placed in the can in which the used irrigating fluid is collected and if the sample is diluted with an equal volume of water before acid is added, the readings are satisfactory, but this needs further study.

It is theoretically possible, too, for a diabetic patient to suffer from the unwanted infusion of an unknown quantity of glucose during a transurethral resection with a glucose irrigating medium, but determinations of the blood sugar before and immediately after operation permits this situation to be dealt with.

Because of the possibility that the fluid used for continuous postoperative irrigation of the bladder may also get into the circulation, sterile half normal saline solution is used for this purpose.

A search for a better fluid for use during operation is in order.

#### SUMMARY AND CONCLUSIONS

1. The hemolysis of blood such as occurs during blackwater fever and after transfusions with incompatible blood or after severe burns leads to hemoglobinemia and hemoglobinuria.

2. If the hemoglobinemia is severe, it may damage the kidney by producing spasm of its vessels, by a direct toxic action, and by the production of pigmented casts which plug the nephron.

3. Intravesical and intravascular hemolysis may be produced during transurethral prostatic resection by the water used as an irrigating fluid. Burning by the current from the surgical diathermy machine may also cause some hemolysis, but this is probably of minor importance.

4. Hemoglobinemia probably does not harm the kidney unless the hemolysis is very severe, or unless the kidney is simultaneously damaged by vaso-spasm from excessive blood loss, by surgical shock, or by the transportation of virulent bacteria from the prostate to the kidney by the irrigating fluid.

5. A hemolytic reaction may be recognized in advance by measuring the free hemoglobin in the plasma at the end of the operation. This is recommended as a routine procedure with transurethral resection. The reaction itself is characterized by nausea, oliguria, a rising urea nitrogen, a mild jaundice, and an anemia out of proportion to the amount of blood actually lost during and after operation. The hemoglobulinuria is masked by the usual post-operative hematuria.

6. The forcing of fluids during and immediately after operation may aid in excreting the hemoglobin with less damage to the kidneys, but after oliguria has appeared, one must be very cautious in administering fluids. Otherwise, treatment consists in trying to keep the patient alive until sufficient time has elapsed to permit recovery of the damaged renal epithelium. Peritoneal lavage may be of some value in achieving this end.

7. The hemolytic reaction can probably be prevented by using an isotonic solution, such as 5 per cent glucose, as an irrigating fluid during transurethral resection of the prostate.

8. A fatal reaction is reported in a case in which sterile water was used as an irrigating agent. Anorexia, hemoglobinemia, anemia, jaundice, and uremia occurred. Peritoneal lavage brought about a remarkable reduction in the urea nitrogen without a diuresis, but death occurred from pulmonary edema.

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## HYPERMOBILITY OF BONES DUE TO "OVERLENGTHENED" CAPSULAR AND LIGAMENTOUS TISSUES

### A CAUSE FOR RECURRENT INTRA-ARTICULAR EFFUSIONS

LIEUTENANT COLONEL CHARLES J. SUTRO, MEDICAL CORPS,  
ARMY OF THE UNITED STATES

THIS paper is based on a study of recurrent effusions of the ankles or knees not associated with known external, local trauma. This was encountered in three white adults from 18 to 35 years old, who had experienced unilateral and occasional bilateral effusions of the knees, and in two others in the same age group, who had suffered from similar involvement of their ankles\*. It was difficult, initially, to explain the basis for the habitual, widespread damage to the joint regions as evidenced by effusion and diffuse tenderness in the absence of any history of pronounced external, local trauma. On further examination or the articulations of these subjects, we observed an abnormal increase in the range of active and passive motion, there was primary hypermobility of the bones at many of the joints of the upper and lower extremities†. It seemed that an "overlength" of certain articular, capsular, and ligamentous tissues was probably the basis for the hypermobility. This laxity had permitted repeated damage to the capsular and ligamentous structures of the joints as a result of minor missteps or sublethal trauma probably suffered during routine physical activities.

With these points in mind, a summary of the clinical and radiographic findings of the five cases is presented. Emphasis is placed on the suggestion that, in the presence of such abnormal ligaments, especially about the knee, conservative therapy should be given an ample trial prior to any contemplated surgical procedure, even if the existence of a joint semilunar cartilage is suspected.

### CLINICAL FINDINGS

*History and Symptoms*—In none of these five cases was there any known evidence of similar involvement of capsular or ligamentous structures of the joints of any member of the immediate family<sup>1</sup>. Three of the patients were not aware of any hypermobility in their articulations prior to entry into the armed forces, although they did suffer in civilian life from occasional enlargement of one or more of the joints of their lower extremities. The other two patients knew that their joints were lax but they had not sought medical aid

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\*Besides these five patients with effusion of the knees or ankles not initiated by externally local trauma, we noted thirteen other white adults from 18 to 35 years old, eleven male and two female, with generalized hypermobility of the bones, each with complaints of pain referable either to the back, neck, knees, legs or feet respectively. In each of these thirteen patients there was a definite external local trauma to the affected part.

†Secondary hypermobility of the bones is usually compensatory to a contiguous ankylosed or rigid joint, for example, marked hypermobility of the bones at the knee is a frequent complication of a fused hip joint.

in civilian life. None of these five patients had suffered from multiple or recurrent fractures of the osseous system as is noted in osteogenesis imperfecta and which is occasionally complicated by hypermobility of the bones.<sup>2</sup> Two of the five patients complained of an increasing number of attacks or swelling, pain, limitation of motion, and weakness of their ankles during the course of military training. The other three experienced similar difficulties with their knees, with symptoms which suggested the possibility of the presence of a torn internal or external semilunar cartilage. In none of the five patients was there simultaneous involvement of the knees and ankles.

*Physical Signs*—Two of the three patients presented unilateral, and one, bilateral, intra-articular effusions of the knees. During the acute, painful stage, the affected legs could not be fully extended or fully flexed because of the existent intra-articular effusion and the presence of spasm of the hamstring muscles. Tenderness was present over the course of the ligamentous structures and especially over the region of the internal or external semilunar cartilages. In the two cases of effusion of the ankles, local tenderness was present when pressure was applied over the region of the lateral and medial ligaments of the articulation. The normal depressions situated anterior to the outer and inner malleoli were partly obliterated. Active and passive plantar and dorsiflexion of the feet was restricted about 10 degrees in each direction, because of pain and effusion. Tenderness was also present in the subtalar and midtarsal regions.

Examination of the other (nonenlarged) articulations of the lower extremities of these patients revealed that a very unusual mobility of the bones existed in the hips, knees, toes, and subtalar regions, and, to a lesser extent, in the ankles. Such hypermobility was also present in the knee joints recently enlarged by an effusion, when re-examined two or three weeks after the onset of this swelling.

Specifically, the examination showed that in three of the five cases the range of total or combined passive abduction of the right and left thighs was from 85 to 105 degrees. These three patients also demonstrated an unusual range of passive extension of the thighs, the greatest angle of extension being from 195 to 210 degrees. Two of these five individuals were able to place their legs on the dorsal aspects of their cervical regions.

Each subject presented an abnormal arc of passive extension of the legs which measured from 190 to 210 degrees at the respective knee joints (Fig. 1). One patient could actively abduct and adduct his legs at the knee joints through a total arc of 15 degrees. This abnormal lateral mobility of the leg caused a temporary alteration in the configuration of the lower extremities from that of a mild knock-knee deformity to that of a bowleg. In four of these subjects there was marked laxity of the patellas to the extent that each could be passively displaced either laterally or medially for a distance measuring about one-half of its diameter. In the fifth, the patellas were so lax that they could be everted so that their articular surfaces were perpendicular to that of the femoral condyles. When the knees of these five patients were flexed at an

angle of 90 degrees, an increase of 5 degrees in the range of passive external rotation of the tibia was also observed. It is of further interest that abnormal, passive, anteroposterior movement of the tibia was found only in one patient, the one with the abnormal lateral mobility of the tibia. The feet of three of the five patients could be passively dorsal and plantar flexed to a total arc measuring at least from 10 to 20 degrees beyond the standard range. In two others, there was definite tautness of the Achilles tendon which restricted dorsiflexion of the feet to an angle of 90 degrees. The arc of inversion of the feet was almost 90 degrees\* as evidenced by the ease with which three of the five patients could oppose the soles and toes of their feet while keeping their knees close together (Fig 2). Furthermore, the foreportion of the feet was unusually lax



Fig. 1.

Fig 1 —Note the abnormal increase in the range of extension of the left leg. This condition was also noted in the right leg.



Fig. 2.

Fig 2 —Note the increase in the range of active inversion of the feet.

and could readily be compressed manually to increase the concavity of the metatarsal head region. Yet in spite of this unusual relaxation, not a single one of these five patients presented a marked depression of the inner longitudinal arches on weight-bearing. One patient had a unilateral relaxation of the deltoid ligament of the ankle which resulted in an eversion of the foot.

Examination also showed that three of the five could flex their trunks so that their chest walls were in close apposition to the anterior aspect of the thighs (Fig. 3). Likewise, these three patients could actively hyperextend their vertebral columns from 30 to 60 degrees dorsally beyond the vertical plane (Fig. 4).

\*Effusion of the ankle may be noted in the presence of "overlengthened" midtarsal ligaments.

Examination of the upper extremities disclosed that in each of three subjects the arms could be hyperabducted to such an extent that the elbows approximated the opposite external ear. In one instance, mild downward traction to the arm caused a subluxation of the humeral head. Passive hyperextension at the elbow was also possible in these five cases and the greatest angle of extension at this articulation varied from 190 to 210 degrees. In addition, in one of these



Fig 3.—Note the unusual range of flexion of the vertebral column.



Fig 4.—Note the hyperextension of the vertebral column.

five patients a definite increase of 10 degrees in the total average range of passive radial and ulnar deviation of the forearm was present. The hands in these five instances could be translocated anteriorly without any difficulty. Passive palmar flexion of these hands was achieved to a point where the palmar aspect of the distal phalanges almost approximated the palmar aspect of the forearms and the tufts of the thumbs could be readily opposed onto the palmar surfaces of the forearms (Fig. 5). All fingers revealed an unusual range of hyperextension and abduction at the interphalangeal and metacarpophalangeal articulations, respectively. The fingers were also extremely hypermobile to such an extent that the metacarpal bone region of the thumb could be placed passively in close proximity to that of the little finger.



Fig. 5—Note the increase in the arc of passive movement of the thumb

One patient in this group of five had a mild laxity of the skin of the face but neither he nor the other four presented a generalized hyperelasticity or cutaneous nodules of the skin as is described in Danlos-Ehler's disease.<sup>4</sup> None of these patients with generalized hypermobility presented any weakness of the voluntary muscles, signs of postencephalitis,<sup>4</sup> "spider fingers,"<sup>13</sup> or any evidence of achondroplasia.\*

*Radiographic Examination.*—In one of these five cases was there any evidence of fracture of the bones of the ankles or knees. Radiographic studies made of the upper and lower extremities in various attitudes confirmed the abnormal range of movement of the bones comprising the articulations as noted in the physical examinations. Radiographs of the knees showed that the range of hyperextension was limited by the apposition of the tibial plateau to the contiguous femoral condyles (Fig. 6). Active lateral adduction of the tibia as

\*We observed hypermobility of the bones comprising the knees of a mother and her 5-year-old daughter, both of whom presented classical pictures of achondroplasia.

noted in one case caused a definite increase in the height of the lateral joint space of the knee joint (Fig. 7). In addition, examination demonstrated that in three instances there was an unusual mobility of the vertebral column in flexion and extension of the trunk.

As far as the upper extremities are concerned, radiographic examination of the shoulder joints disclosed that in the hyperabducted position of the arm, the greater tuberosity of the humerus was contiguous to the inferior lip of the

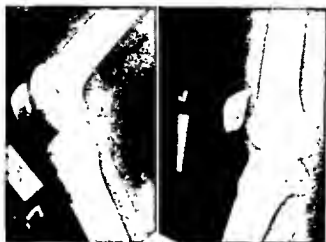


Fig. 6.—Radiographs showing the knee in flexion and in hyperextension. Note the apposition of the anterior portion of the tibial plateau to the femoral condyles.



Fig. 7.



Fig. 8.

Fig. 7.—Radiographs demonstrating the relative increase in the joint space in the outer half of the right and left knees. This patient was able to abduct and adduct his legs actively.

Fig. 8.—Radiograph of shoulder region shows the extreme range of abduction of the humerus. The greater tuberosity of the humerus is at the level of the inferior rim of the glenoid.

glenoid of the scapula (Fig. 8). Subluxation of the humeral head was noted on mild downward traction of the arm.

Passive hyperextension at the elbow joint was also observed in these radiographic studies. The increase in the range of passive palmar and dorsiflexion



Fig. 9



Fig. 10

Fig. 9--Radiograph of hand shows unusual range of active abduction and adduction of the fingers.

Fig. 10--Radiograph of hand demonstrates a typical fixed "windmill sail" position of the fingers.

of the hand was reflected by an unusual range of mobility of the capitate bone. There was also an extreme range of active and passive abduction of the fingers and this occurred chiefly at the metacarpophalangeal articulation\* (Fig. 9).

\*Two additional cases not included in this series were studied which presented a fixed ulnar deviation of all the fingers, probably secondary to an anomaly of the metacarpal bones and of the ligamentous structures of the metacarpophalangeal articulations. The abnormal attitude of these fingers could not be fully corrected by either passive or active manipulations. Radiographic studies revealed that the proximal phalanges of these fingers articulated with only part of the metacarpal heads (Fig. 10). It is of interest that in one of the five cases of primary hypermobility in this series, we noted a mild degree of fixed ulnar deviation coexistent with a definite increase in the range of passive extension of the fingers. The abnormal, fixed, ulnar attitude of these digits has been designated as a "windmill sail deformity". This must be sharply differentiated from acquired abnormal contractures caused by infectious processes of the joints of the hand.



## TREATMENT

The general course of treatment for effusions of the ankle or knee was bed rest and application of cold or warm compresses to the painful part. Traction was instituted to the leg in order to relieve the spasm of the hamstring muscles. Aspiration of the articular cavity was performed if the effusion obliterated all landmarks. When the pain subsided, nonweight bearing resistance exercises were initiated to strengthen the quadriceps muscles. An elastic bandage was placed about the ankle or knee to permit weight bearing as soon as the effusion had disappeared. Approximately seven to fourteen days of traction resulted in a complete relaxation of the spasm of the hamstring muscles. In order to prevent recurrence of the effusion and pain, the use of an elastic support with concomitant muscle training was stressed. Although it appeared logical that in certain instances treatment should have been directed toward shortening or retraction of the abnormal ligamentous structures, such procedures were not pursued in this study. Some of the patients were reassigned to special duties which did not require excessive use of their lower extremities and others were separated from the armed forces when no adequate positions were available.

## DISCUSSION

There has been no available material for microscopic study to determine whether there is an actual increase in elastic tissue content of the ligaments or capsules in cases of hypermobility of bones. We suspect that the basic abnormality is an intrinsic "overstretching" of the entire ligaments and capsules with a secondary disturbance of the normal elastic constitution. While relaxation and secondary loosening of the ligaments is common as that covering the patella symptoms can be experimentally induced in normal animals by subcutaneous injections of estradiol benzoate or by oophorectomy during the latter period of pregnancy. We could find no evidence of evidence of any hormonal disturbance in these five patients.

It appears that a probable cause for hypermobility is a disproportion in the relative rate of growth of the bones and ligaments and ligaments.\* Thus, an excess of ligament elasticity leads to hypermobility and in turn to rigidity of the bones comprising the articulation.

Recognition of the status of the ligamentous and capsular tissue is of value especially in the planning of treatment of effusions of the knee joint. In three

cases of recurrent effusion of the knees not associated with trauma and in the other instances of hypermobile knees associated with trauma, the existent symptoms and signs simulated that caused by a torn internal or external semilunar cartilage. These are the patients in whom arthrotomy should be postponed until conservative therapy and a change in duty have been given a fair and reasonable trial. Where arthrotomy was done in two instances of recurrent effusion and hypermobility of the knee associated with external trauma, we noted the presence of fissures in the articular cartilage of the patella and no evidence of a torn or displaced semilunar cartilage. In considering the various causes for protracted effusion of the knee, as infectious arthritis, osteoarthritis, intermittent hydroarthrosis, or effusions associated with syphilis, one should not overlook hypermobility of the bones at the articulation.

Recurrent effusions of the ankle either with or without trauma in the presence of "overlengthened" ligaments of the ankle joint or of the midtarsal region should be treated by a trial of conservative methods as ankle supports, strapping, and muscle exercises. Change in duties which limits the use of the lower extremities is an essential part of the treatment in such cases.

It must be emphasized that hypermobility may be the cause for low back pain, cervical rib syndrome, flat feet, and the basis for recurrent subluxation of the intercarpal region, humeral head, or patella. In any event, surgical intervention is indicated for correction of the subluxation in instances of recurrent, protracted, disabling, frank subluxations of the astragalus, carpal bones, humeral head or patella when associated with or without hypermobility.

#### CONCLUSION

In five patients with "overlengthened" capsular and ligamentous structures of the joints of the upper and lower extremities (primary hypermobility of the bones) we noted the presence of recurrent effusions of the ankles or knee joints in the absence of pronounced external, local trauma. The hypermobility of the bones at the joints permitted the occurrence of subclinical traumas to these parts, especially following prolonged periods of weight-bearing as pursued in military training. When the knees were involved, the symptoms and signs simulated that caused by a torn semilunar cartilage. In the presence of hypermobility of the bones, conservative therapy should be given a fair trial before contemplation of arthrotomy of the knee for removal of a semilunar cartilage. A change in duty restricting excessive use of the knees may prevent recurrent effusions.

The etiology of the "overlengthened" ligaments is unknown. No clinical evidence of any hormonal disturbance could be established. In these five instances no evidence of generalized hyperelasticity of the skin or anomaly of the skeleton was noted.

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## TREATMENT

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It appears that a probable cause for hypermobility is a disproportion in the relative rate of growth of the bones and their attached ligaments.\* Thus, an excess of ligament could lead to hypermobility, and an insufficiency to rigidity of the bones comprising the articulations.

Recognition of the status of the ligamentous and capsular tissue is of value especially in the plan of treatment of affections of the knee joint. In three

\*As a correlative study we examined the range of motion of the joints of 235 young male adults from 18 to 35 years who were patients in the orthopedic wards. We noted that ten patients or 4 per cent of the group presented evidence of hypermobility of three or more pairs of joints without any concomitant hyperelasticity of the skin. Two of these ten patients had unilateral, recurrent subluxation of the humeral head and a third had severe flat feet. The remaining seven patients showed orthopedic lesions, as fractures etc. not specifically related to the hypermobility of the bones. In these 235 patients, six showed localized hypermobility of the knees, twenty-nine, of the thumbs, and eight of the ankles. At this time those with localized hypermobility of the knees, thumbs or ankles had no complaints referable to these parts.

A study was also made of the movements of the joints of twenty-five newborn infants. It was interesting to observe the universal wide range of passive dorsiflexion at the ankles which permitted approximation of the tufts of the toes to the legs. Furthermore, in all of these infants, the tufts of the thumbs and of the fingers could be made to touch the palmar aspect of the forearms. No instances of hypermobility at the knees were encountered. Examination of twelve children aged from 2 to 8 years revealed that hypermobility of the thumb and fingers was noted in six instances and that hypermobility in the knee joints was present in three cases.<sup>8</sup> This limited study suggested that in certain stages of development of the skeleton the rate of bone growth may not be parallel to that of the ligamentous and capsular tissues. This may lead to a relative excess or insufficiency of ligaments with either laxity or rigidity of the bones comprising the joint.

## VASCULAR WOUNDS

### REPORT OF A SERIES OF 108 CASES ENCOUNTERED IN A FORWARD EVACUATION HOSPITAL

LIEUTENANT COLONEL JOHN M. SNYDER, ARMY OF THE UNITED STATES

THE experiences and impressions herein related are derived from observance of approximately 25,000 wounded treated by the evacuation hospital in which the author was fortunate enough to serve as chief of the Surgical Service.

When the unit landed with the invasion forces in North Africa, the literature on management of vascular injuries was not profuse. A number of axioms had been handed down from World War I, and the Spanish Civil War had furnished some further experience. The Manual of Therapy as compiled by the Surgeon General's Office and The National Research Council resolved the previous experience into axiomatic summary as follows (1) Companion vein ligation; (2) ligation, if possible, immediately caudad to the last large branching vessel above the injury.

Although the field of vascular surgery may seem at times to be too specialized to be of general interest, when vascular complications of injured extremities do suddenly confront the surgeon, a ready appreciation of the sequelae of injury at various levels may well aid in deciding between a conservative or more radical type of management. Since the preservation of life in a limb is probably determined within a very few hours after injury, it is well to try to examine and evaluate the experience of war where injuries of the extremities form such a large proportion of those wounded, so that this may be recorded for future reference, as well as for its possible pertinence to civilian practice in effecting, if possible, a higher salvage of the badly injured extremities so often encountered in industrial as well as highway and other transportation accidents.

In the North African invasion, the majority of wounded suffered from injury by small arms fire, and vascular complications requiring amputation for decreased blood supply were relatively few. In the subsequent Tunisian campaign, land mine injuries often resulted in traumatic amputations at levels below the knee, but again vascular injuries were not too numerous. During this campaign sixteen patients were treated for gas gangrene. In twelve of these, the infection developed in limbs where injury rendered the distal limb avascular, or relatively so, and while attempting to save it by sympathetic blocks and vasodilatory drugs the anaerobic infection supervened. This, then, became one of the major complications of vascular injury, but since its incidence was relatively small and war surgery so completely new to those of my unit, the seemingly more dramatic abdominal<sup>1</sup> and chest wounds<sup>2</sup> were more thoroughly scrutinized and reported. However, in approximately 4,000 wounded

treated by us in the North African, Tunisian, and Sicilian campaigns, roughly 81 per cent had extremity wounds and about one per cent had amputations. DeBakey<sup>3</sup> has recently summarized the Army experience for the war. In 163,980 battle casualties, arterial wounds occurred with an incidence of 1.4 per cent, and were the cause for amputation in 19.4 per cent of those amputations performed. Inversely, of 2,300 arterial wounds, 40 per cent required amputations.

Upon arrival in Normandy, D Day plus 4, the unit was flooded with casualties, handling over 6,000 in the first thirty-one days and operating upon 4,000 of these. Wounds of the extremities occurred in 74.4 per cent of the wounded, and amputations were required in 1.1 per cent of the extremity wounds, usually because of avascularity. Observation and review of these injuries soon revealed a rather constant series of conclusions, of which the most obvious and constant was gangrene involving the lower three-fourths of the leg (below the knee) in popliteal injuries. In three patients with severe posterior dislocation of the knee joint, encountered early in the African campaign, popliteal injury had occurred in two, with loss of the distal limb from gangrene.

With the increasing frequency or incidence of vascular wounds, and the too constant, distressing results of passive therapy, a more energetic regime was instituted, with careful records of the results. The greatest incidence of major vascular injuries thus handled occurred during the battle of the Ardennes. Thereafter, the relative incidence seemed to decrease. Monthly records were kept, and bore out this observation.

For the sake of easier discussion, the injuries will be discussed in sequence of their anatomic location cephalad to caudad. The management will be discussed following the record of the cases. The series includes 108 patients on whom records were kept, 106 of whom were operated upon, the other two being conservatively treated for arteriovenous fistulae.

The most interesting of these vascular wounds were those involving major arteries. Ninety of the series were treated during the battle of the Ardennes, which was actually between Dec 10, 1944, and Jan 22, 1945. Conservation was the keynote of the management, although individual variations in technique did occur as the result of the relatively large number of surgeons operating in the unit (twenty-two). In the great majority of patients, loss of vessel substance was too great to allow anastomosis, with Blakemore tubes not being available for vein transplants, nor anticoagulants for preventing thrombosis subsequently. Many times, anastomosis seemed at first feasible until closer examination revealed the intima to be destroyed a considerable distance beyond the apparent loss of media and adventitia.

The principles of management striven for were maximum preservation of circulation by vascular reconstruction if possible, by routine sympathetic block every twelve hours, by reduction of the metabolism of the extremity to a minimum by cooling. In the case of cervical sympathetic blocks, the anterior approach seemed more satisfactory, with a positive Horner's response produced much more frequently.

The following observations cover 108 cases. The most cephalad injury involved an external carotid which required ligation, without sequelae. Exclusive of a patient with arteriovenous fistula treated conservatively, there were, in addition, forty-six cases involving major vessels of the upper extremity. The most major injury of these involved both subclavian artery and vein. A soldier's Tommy-gun accidentally discharged twice in rapid succession, both bullets entering the left chest at the same level just above the nipple, approximately one-half inch apart, and leaving posteriorly above the scapular ridge about one inch apart, again at the same level. Compression and transfusion controlled the patient's condition during preparation for operation. Under general anesthesia, the subclavian was controlled after being exposed by subperiosteal resection of the proximal third of the clavicle. Almost immediately following placing of the control tape about the vessel proximal to the wound, the thrombus which had formed in the vessel's end let go, but the bleeding was under satisfactory control. About an inch of artery had been shot away, as well as all of the subclavian vein from its junction with the internal jugular to its axillary portion. The artery was tied proximally and distally. Immediately thereafter the distal portion was seen to fill with blood, indicating adequate circulation. The vein was ligated at the jugular and distally. The extremity remained warm. Motor and sensory loss were present from the time of injury although the brachial plexus grossly appeared uninjured at surgery, and paresthesias developed after several days.

There were also three cases of injury to the axillary artery at a high level, one being encountered in the European campaign, in which both artery and vein were ligated and divided and circulation remained adequate. A second but earlier case of high axillary artery loss was encountered during the Sicilian campaign. About an inch of the vessel had been shot away. The artery was ligated proximally and distally. The companion vein was ligated and divided. The patient developed considerable edema and, eventually, slight gangrene of the finger tips. This earlier case had not had as many or as energetic cervical sympathetic blocks, and these had been done by the posterior instead of the anterior approach.

The third axillary artery injury required ligation in the distal third. The companion vein was not ligated, and the patient developed slight dry gangrene of the tip of the thumb and middle finger.

There were twenty-seven patients with injuries to the brachial artery. Seven had injuries above the level of the origin of the profunda. An eighth similarly injured, will be discussed separately. Five of these injuries were ligated and two were repaired. In two of those ligated, with an associated humeral fracture, gangrene developed in the forearm complicated by rapidly advancing gas bacillus infection, and emergency high amputation was necessary. One of these patients died of pulmonary embolus later. The eighth patient thought to have been injured at approximately this level with an associated compound fracture, was debrided in a field hospital, given two stellate ganglion blocks for a cold extremity, and brought to the evacuation hospital four days later. Gas gangrene developed shortly, despite further cervical

sible are imperative, and that even if secondary thrombosis of varying degree seems likely, a temporary reprieve from avascularity may give enough time for increased collateral circulation to develop, perhaps enough to save an additional joint, if not the limb. This may possibly follow a secondary decrease in the edema originally resulting from injury, or relaxation of vasospasm after a number of hours, either or both allowing increased vascular flow to the extremity.

In marked contrast to the series of wounds above the level of the origin of the profunda femoris, wounds of the femoral artery immediately below the profunda, the latter being intact, have a much better prognosis. There were fifteen patients in this category. One patient had two inches of femoral artery shot away shortly distal to the profunda. At the time of surgery his distal extremity was warm and remained so after ligation. Circulation remained adequate. It has been our experience that if the limb is immediately warm though pulseless after ligation, by rest, cooling, and sympathetic blocks it can be saved despite ligation. There were three patients with lacerations of the femoral artery, two of which lacerations involved three-quarters of the circumference. A dorsalis pedis pulsation was palpable after repair in two of the three patients, but circulation remained adequate in all. A fifth patient presented a warm foot but no demonstrable peripheral pulsations after removal of a thrombus of the artery at this level (distal to the profunda), the foot having been cold before surgery. The extremity remained viable. One other patient with a thrombus presented a warm foot initially, so the thrombus was not removed. The companion vein, having been lacerated, was ligated. The circulation remained adequate. The remaining nine femoral artery injuries in this group required ligations of the artery and vein. Three were upper third injuries (just below the profunda) without a sequelae. A fourth injury at almost the same height, however, resulted in eventual gangrene of several toes, though there seemed no doubt about being able to save the foot. Two cases of injury to the middle third resulted in gangrene; one limb demarcated at the ankle level and one at mid-calf level. Three patients with injury in the lower third presented widely different sequelae, however. One of these, with level of injury in Hunter's canal, had inadequate circulation for the toes and forefoot. The second, with the vessel ligated at the lower end of the adductor canal as it emerged lateral to the adductor muscle, had no circulatory inadequacy, and the foot remained pulseless but warm. The last of the three, with both artery and vein lacerated at this same level, developed a cold limb to the level of injury and will eventually need a mid-thigh amputation (the sequelae commonly following popliteal injury).

There were four cases where the profunda femoris was ligated, all without sequelae.

Light popliteal artery injuries occurred. Thrombosis followed anastomosis in one patient, and amputation was carried out at the fracture site level, the knee. Another patient with compound fracture of both bones and popliteal injury at the level of the fibular head, had no sequelae.





sympathetic blocks, and required high amputation. Two days later the patient died an embolic death. In the three remaining patients, ligated under the regime of cooling and cervical sympathetic blocks at twelve-hour intervals, all demarcated and went on to dry gangrene, one at the metacarpophalangeal level, another just above the wrist, and the third just below the elbow. The two patients whose vessels were repaired had lacerations involving three-fourths of the circumference. Following repair, both of these patients regained radial pulses and maintained adequate circulation to the extremity, later being evacuated in good condition.

Of the nineteen brachial artery injuries below the profunda, three had vascular repairs: one of these latter had thrombosis in an intact vessel, secondary to a missile passing close by. After removal of the thrombus and vessel repair there was a brief, questionable pulse but circulation remained adequate. A complete brachial artery severance was repaired by anastomosis. Although no radial pulse returned, circulation remained adequate. The third repair, of a laceration involving only one quarter of the vessel circumference, likewise failed to effect a return of the radial pulse. The hand remained cool, and there seemed a possibility that some fingers would need later amputation, though after ten days this was still uncertain. The results in the remaining sixteen cases of ligation cast doubt that survival in the above can be in any way ascribed to the repair. One patient with the brachial tied just below the profunda retained uncompromised circulation. In eleven patients with severance and ligation of the vessel in the middle third of the arm, there were only two with insufficient collateral blood supply to the distant extremity, both proceeding to dry gangrene. One subsequently must have lost much of his hand and the other probably required amputation later, in the lower third of the forearm about the wrist. The remaining four patients had interruption of the blood supply in the distal third of the arm. One patient with level of injury two inches about the elbow developed a dry gangrene and probably required later amputation in the upper third of the forearm. The other three fared much better. One patient with the artery divided just above the bifurcation into the radial and ulnar arteries developed a dry gangrene of the finger tips. A second with a thrombus at the same level had a cool hand but seemed well on the way to saving all of it. The last of the three, with level of injury at the elbow joint, had no circulatory inadequacy.

There were fifteen patients with ligation of the radial, ulnar, or both arteries: seven radial, five ulnar, and three combined, one of the latter being at the wrist level. Circulation was adequate in all patients.

There were fifty-nine patients with injury to major vessels of the lower extremities treated operatively, including one fatal injury involving the right common iliac at the aortic bifurcation. Attempted repair failed, and the surgeon was forced to ligate above the site of injury. The patient died of shock twelve hours after surgery, with limbs avascular.

Injuries of the external iliac artery occurred twice. In one, the vein had been shot away and the artery thrombosed for a distance of 6 or 7 cm, with vessel wall black from extravasated blood. The thrombus was twenty-four

hours old at time of operation, and firmly adherent; the vessel was nonviable, so it was ligated and divided. Amputation was later performed at the lower third of the thigh. The other patient was brought to the hospital four days after wounding and three days postoperative (Field Hospital) of a cystostomy following a fractured pelvis with early gangrene of right thigh and leg below the inguinal ligament. At amputation five days later the vessel injury was found to be at the level of the external iliac, the hypogastric being apparently intact. Circulatory interference was so extensive that disarticulation of the hip was finally necessary.

One patient had a severe wound of the external iliac vein immediately distal to the junction with the hypogastric, but no arterial injury. Exact location of the injury was determined during an intra-abdominal operation for associated intestinal wounds, and it was readily controlled by an extraperitoneal ligation distal to the injury. This was accomplished quite simply and rapidly by exposure of the iliac vessels above the inguinal ligament through a separate incision. This method of approach is advocated for control of high femoral artery injuries, in order to place a preliminary prophylactic control tape before exposure of the actual arterial injury.

In the series there were three patients with femoral artery injury above the profunda femoris. One had thrombosis of the femoral artery at this level. The vessel was opened, thrombectomy performed, and the vessel repaired. The foot, which was cold before operation, was now warm, although no pulse could be detected. Circulation remained adequate. My only explanation is that removal of the thrombus allowed the vasospastic reflex to be ameliorated and responsive to lumbar sympathetic blocks, and mural thrombosis about the injured intima did not completely occlude the vessel, or, by the time it did, collateral circulation became adequate. Pathogenesis of the original thrombus will be discussed later. The second femoral injury was in a patient with extensive loss of both artery and vein, extending at least 1.5 cm above and below the origin of the profunda. Ligation was the only procedure which could be carried out quickly in a gravely injured patient. A high thigh amputation would have been necessary had he not succumbed the second postoperative day to a cerebral blast effect. The third of these high femoral injuries occurred in a prisoner of war, with loss of  $1\frac{1}{2}$  inches of femoral artery proximal to the profunda femoris. About  $1\frac{1}{2}$  inches of femoral vein was transplanted and anastomosed to fill the defect. Posterior tibial pulsations were present at the ankle for a little over twelve hours after surgery. As there was no anticoagulant available, secondary thrombosis supervened, and arterial emboli broke off, one lodging further distally in the posterior tibial artery, producing severe pain in the calf of the leg. A line of demarcation at the ankle eventually developed. In view of the results of ligation in patients with external iliac and other femoral injuries at this level, this is a very illustrative case. Patients with interruption of the arterial supply proximal to the origin of the profunda femoris usually have demarcation above the knee, despite all sympathetic blocks and other supportive measures. It would thus seem that in wounds proximal to the profunda, all possible reconstructive measures pos-

sible are imperative, and that even if secondary thrombosis of varying degree seems likely, a temporary reprieve from avascularity may give enough time for increased collateral circulation to develop, perhaps enough to save an additional joint, if not the limb. This may possibly follow a secondary decrease in the edema originally resulting from injury, or relaxation of vasospasm after a number of hours, either or both allowing increased vascular flow to the extremity.

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## SURGERY

### CONCLUSIONS

From the foregoing series of cases, a number of observations seem pertinent:

1. The critical sites of injury are mainly the brachial artery and femoral arteries above their respective profunda branches, and also the external iliac and popliteal arteries. Kirtley,<sup>4</sup> reporting vascular injuries seen in a general hospital in a theater of observations, noted that 20 per cent of the amputations were for circulatory causes, with about one-half following popliteal injury and approximately one-third following femoral artery injury.

2. Ligation below the critical sites here mentioned, in the absence of extensive wounds and tissue damage interfering with collateral circulation, will generally not result in loss of the extremity.

3. At the critical sites, every effort should be made at repair by silk and/or by vein transplant, including thrombectomy even in the absence of anticoagulants, vitallium, or plastic tubes (Blakemore), as the temporary partial sustenance of circulation to an extremity after anastomosis may be adequate for maintenance of a viable extremity, or, if secondary thrombosis does occur, it may allow sufficient time for the collateral circulation to develop enough to allow final gangrene demarcation level to be at least distal to a joint which might otherwise have had to be sacrificed. Kirtley<sup>4</sup> reported three popliteal injuries with Blakemore tube repairs with a viable foot, if not in toto, in part, although the anastomosis had thrombosed. Of twenty-nine patients with popliteal injuries, three of the four maintaining viable extremities had had lumbar ganglionectomies, the fourth, lumbar sympathetic blocks. Statistically, DeBakey<sup>3</sup> reports that various methods of repair, including the use of the vitallium tube, gave no reduction in percentage of amputations required.

4. In our experience, sympathetic blocks and lowering of the metabolism of the extremities by cooling during the postoperative salvage period increase the amount of limb saved and favor the development of a dry rather than a wet gangrene. Shant elevation, enough to favor gravity drainage, also favors the development of a dry gangrene, and has, at times, seemed to be quite helpful in converting a moist to a dry gangrene.

5. The incidence of pulmonary embolism is appreciable in extensive injuries to the extremities involving the major vessels. The incidence of embolism seems particularly unfortunate after secondary amputation for gangrene. The need for all possible prophylactic measures is obvious.

6. In the presence of associated major fractures, collateral circulation is likely to be less able to furnish adequate sustenance for the injured limb, and the prognosis is influenced accordingly.

7. In injuries to major vessels, and frequently in cases of explosive missiles passing close by, thrombosis of major arteries is very common. In severed vessels this may be temporarily lifesaving and allow sufficient time for a temporary proximal control tape or ligature to be placed. This latter preliminary procedure is mandatory in the management of major vessel injuries where repair is contemplated, at the same time saving the patient from unnecessary loss of blood during débridement.

8. In all major extremity wounds, the status of the circulation should be immediately recorded and carefully watched throughout the operative and postoperative period. A warm extremity is always a good prognostic sign, even though pulsations are absent.

9. When major vessels must be ligated, as suggested by Holman,<sup>5</sup> if ligation is performed as close distally to the last proximal major branching vessel as possible, the chance of maximum collateral response seems greatest.

#### SUMMARY

In conclusion, the experiences with wounds of the major vessels of the extremities as encountered in a war-combat zone have been detailed. It is felt that with all the industrial and highway accidents which occur in this country, the experiences being related may be translated with profit to the field of traumatic civilian surgery.

A series of conclusions or pertinent observations have been listed

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upon the skin; they are connected with a line of the dye. Thus, a replica of the defect has been traced upon the donor area within a period of about three minutes. The incision may then be made outside the line according to how much larger it is desired to cut the graft—usually  $\frac{1}{16}$  to  $\frac{3}{16}$  inch—to make the graft somewhat larger than the pattern.

When the graft is dissected from its donor site, every morsel of subcutaneous fat is removed from its undersurface; in fact, a bit of the corium is commonly removed in order to be certain. After dissecting it up with rather bold strokes of a sharp scalpel, we find that sharp straight scissors provide the most efficient means of removing the remaining bits of fat. Complete hemostasis is, of course, a necessity. This can be facilitated in both donor and recipient areas if incision and dissection are preceded by injection with normal saline solution or 1 per cent novocain solution containing a few (usually 3 to 8) drops of adrenalin per ounce. When a vessel must be tied, we prefer very fine silk or cotton to catgut; it has been amply demonstrated that the latter is the most irritating of these materials. The graft should be secured in its recipient site by placing sutures at salient points so that tension will be equally distributed as the remainder of the edge is closed. Interrupted sutures should be used throughout, preferably about  $\frac{1}{8}$  inch apart with the knots outside the suture line and one end of the sutures left long to tie across the stent or first layer of gauze.

It may be a temptation to save time by the use of widely spaced interrupted sutures and to finish the closure with a continuous stitch. However, all interrupted sutures picked up in groups of two to four and tied across a stent or gauze pad assure uniform pressure and evenly distributed gentle tension. This results in a better scar line where graft and recipient edge unite; it is well worth the small amount of effort and extra time.

While the surgeon is applying the graft, the gauze bearing the tracing can be used by the nurse as a guide in preparing the dressings which will be used immediately over the graft. Unless a mold or stent of modeling compound is to be a medium of pressure, a pad of gauze should be cut to conform to the graft and to constitute the initial portion of the dressing. Next to the graft there should be a single thickness of fine mesh dry or slightly greasy gauze, which has minimal tendency to adhere to the graft. Then the pad of gauze moistened with normal saline solution is laid on and sutures tied across it, thus establishing uniform and dependable pressure.

If there has been any oozing from the recipient bed, a syringe of saline solution may wash away any clots or thin layer of blood just before the pressure is applied. A coarse needle inserted between the stitches will facilitate this step and cause no loss of time.

A "rope" of moist gauze is wound around and tucked into the small space between the edge of the molded dressing, slightly drawn up by the long ends of sutures tied over it, and the surrounding skin. Moist gauze is more absorbent than dry gauze and obviates the possibility of a dead space or of exudate accumulating, fouling the suture line and permitting stitches to cut in. Larger pads of gauze or mechanic's waste are laid upon the sutured dressing, followed by

additional firm but gentle even pressure assured by taping and elastic or resilient bandages. We have found that bandages prepared by sectioning long rolls of stockinet on a bias are incomparable as a means of providing optimum pressure.

In some locations—as the nose, cheek, upper or lower lip—very bulky dressings are impracticable. In these instances, corset types of dressing are made with strips of adhesive tape upon the neck and cheeks, doubled over at the end closest to the graft and, with a hole through the tape, bandage is tied or laced over the outside covering of the grafted area. In many instances for the nose, lips, or cheek, gauze bandage secured to the ends of the tape and tied behind the neck is helpful.

Pressure is easily procured about the eyes, forehead, or ears by the usual turban type of circumferential bandaging; pressure is accurately gauged by varying the tension on two short strips of gauze laid vertically against the skin preceding the circumferential wrapping; when they are tied around the turban perpendicularly the appropriate amount of pressure is estimated.

Tincture of benzoin applied to skin or to the vermilion edge of a lip will facilitate adhesion of the tape and maintenance of dryness by diverting secretions of the mouth or nose.

Special comment upon eyebrow grafts is fitting at this point. Incidental to treatment of many severe facial burns, this problem has arisen many times. We have stated that the free graft is utterly dependent upon its base, rather than its edges, for nutrition. A probable exception to this is the scalp graft for making an eyebrow. It is a familiar fact that the hair or hair roots within the graft, at the time of transfer, usually are shed. Then a certain per cent of the follicles survive and produce new hair. It is noted that often more hairs survive near the borders of the graft, and a higher per cent survive in a slender graft than in a wide one. Knowing that bold thinning on the deep side of this graft destroys many hair follicle bulbs, we find that less bold thinning and a narrower graft begot a greater per cent of viable follicles. These observations indicate that substantial nutriment reaches the graft from its side. Two or three long narrow grafts, placed side by side at intervals of ten days or more, result in survival of more hairs—especially if the knife blade is inserted into the donor area and drawn parallel to the hair shafts while taking the graft.

#### POSTOPERATIVE CARE

Patients having had grafts to the chin or upper or lower lip receive nothing by mouth except liquids through a straw to minimize movement and maintain dryness for about one week. Penicillin, 25,000 units intramuscularly every three hours, is given routinely to all face grafts—and in any other case where local, systemic, or extraneous sepsis might constitute a threat—as an additional measure of precaution against infection. This is given until the time of initial dressing or until aseptic healing is assured. Dressings on face grafts are usually left undisturbed for five days, by which time stitches must be out to avoid marks. During this five-day period, the dressings are checked daily to insure adequate pressure and prevention of soiling from nasal or oral secretions.



upon the skin, they are connected with a line of the dye. Thus, a replica of the defect has been traced upon the donor area within a period of about three minutes. The incision may then be made outside the line according to how much larger it is desired to cut the graft—usually  $\frac{1}{16}$  to  $\frac{3}{16}$  inch—to make the graft somewhat larger than the pattern.

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While the surgeon is applying the graft, the gauze bearing the tracing can be used by the nurse as a guide in preparing the dressings which will be used immediately over the graft. Unless a mold or stent of modeling compound is to be a medium of pressure, a pad of gauze should be cut to conform to the graft and to constitute the initial portion of the dressing. Next to the graft there should be a single thickness of fine mesh dry or slightly greasy gauze, which has minimal tendency to adhere to the graft. Then the pad of gauze moistened with normal saline solution is laid on and sutures tied across it, thus establishing uniform and dependable pressure.

If there has been any oozing from the recipient bed, a syringe of saline solution may wash away any clots or thin layer of blood just before the pressure is applied. A coarse needle inserted between the stitches will facilitate this step and cause no loss of time.

A "rope" of moist gauze is wound around and tucked into the small space between the edge of the molded dressing, slightly drawn up by the long ends of sutures tied over it, and the surrounding skin. **NOTE:** gauze is more absorbent than dry gauze and obviates the possibility of a dead space or of exudate accumulating, fouling the suture line and permitting stitches to cut in. Larger pads of gauze or mechanic's waste are laid upon the sutured dressing, followed by

additional firm but gentle even pressure assured by taping and elastic or resilient bandages. We have found that bandages prepared by sectioning long rolls of stockinet on a bias are incomparable as a means of providing optimum pressure.

In some locations—as the nose, cheek, upper or lower lip—very bulky dressings are impracticable. In these instances, corset types of dressing are made with strips of adhesive tape upon the neck and cheeks, doubled over at the end closest to the graft and, with a hole through the tape, bandage is tied or laced over the outside covering of the grafted area. In many instances for the nose, lips, or cheek, gauze bandage secured to the ends of the tape and tied behind the neck is helpful.

Pressure is easily procured about the eyes, forehead, or ears by the usual turban type of circumferential bandaging; pressure is accurately gauged by varying the tension on two short strips of gauze laid vertically against the skin preceding the circumferential wrapping; when they are tied around the turban perpendicularly the appropriate amount of pressure is estimated.

Tincture of benzoin applied to skin or to the vermilion edge of a lip will facilitate adhesion of the tape and maintenance of dryness by diverting secretions of the mouth or nose.

Special comment upon eyebrow grafts is fitting at this point. Incidental to treatment of many severe facial burns, this problem has arisen many times. We have stated that the free graft is utterly dependent upon its base, rather than its edges, for nutrition. A probable exception to this is the scalp graft for making an eyebrow. It is a familiar fact that the hair or hair roots within the graft, at the time of transfer, usually are shed. Then a certain per cent of the follicles survive and produce new hair. It is noted that often more hairs survive near the borders of the graft, and a higher per cent survive in a slender graft than in a wide one. Knowing that bold thinning on the deep side of this graft destroys many hair follicle bulbs, we find that less bold thinning and a narrower graft begot a greater per cent of viable follicles. These observations indicate that substantial nutriment reaches the graft from its side. Two or three long narrow grafts, placed side by side at intervals of ten days or more, result in survival of more hairs—especially if the knife blade is inserted into the donor area and drawn parallel to the hair shafts while taking the graft.

#### POSTOPERATIVE CARE

Patients having had grafts to the chin or upper or lower lip receive nothing by mouth except liquids through a straw to minimize movement and maintain dryness for about one week. Penicillin, 25,000 units intramuscularly every three hours, is given routinely to all face grafts—and in any other case where local, systemic, or extraneous sepsis might constitute a threat—as an additional measure of precaution against infection. This is given until the time of initial dressing or until asep<sup>ic</sup> healing is assured. Dressings on face grafts are usually left undisturbed for five days, by which time stitches must be out to avoid marks. During this five-day period, the dressings are checked daily to insure adequate pressure and prevention of soiling from nasal or oral secretions.



Fig. 1



Fig. 2

Fig. 1—Severe third degree burns of face imperfectly healed with one split-skin graft and fragile hypertrophic scar.

Fig. 2—Large Wolfe grafts in cheek, lips and chin. Ear is being restored with preserved cartilage of t-skin graft behind, and tubed supraclavicular graft.



Fig. 3.



Fig. 4

Fig. 3—Characteristic ectropion of lips due to burn contracture.

Fig. 4—Correction by Wolfe grafts.

Dressings down to those tied directly over the graft may be changed at any time, if necessary to maintain immobility, pressure, and dryness. Elsewhere, as on the hand, dressings upon Wolfe grafts may be left undisturbed for ten days or so.

Early removal of dressings and stitches should be done with the same meticulous care used at the operation in order to prevent any detachment of the graft or separation of its edge. The sutures are cut and teased away from the stent or the gauze, by now firmly molded to the area; then the mold is teased away from the graft, starting at one end. With a forceps holding the mold, the graft can be gently pushed away a bit at a time until separated, disturbance of the graft is thus avoided. This maneuver is facilitated by inserting and opening narrow-bladed scissors between the graft and the gauze. The mold is set aside on sterile gauze for reapplication if it has remained dry and clean; it conforms exactly to the graft and is thus an excellent medium for reapplication of pressure.

All sutures, as a rule, are removed at the initial dressing, especially upon the face, carefully avoiding separation of graft and recipient edge. Edges of the graft are best cleaned with hydrogen peroxide, dried, and 20 per cent mercurchrome solution is applied as a drying and bacteriostatic agent. This is especially important if any moisture is present about the edge. A successful graft at this time presents a pink color.

Reapplication of pressure upon the graft following cleansing and treatment of any complications (to be mentioned later), when present, resembles the original dressing at the operating table. A layer of fine mesh gauze, which does not tend to stick, and the original gauze mold in its exact previous position are replaced. There is no need now for greasy gauze. In fact it is best avoided, because the prolonged presence of a greasy substance encourages inaccreration and incubates any residual bacteria in a warm, moist, and nutritious medium inevitable in secretions or decomposing tissue. This mold, usually hardened by the serum exuded and original saline solution and capable of re-establishing perfect uniform pressure, is to be reapplied. A strip of tape across it will fix it "home" as gentle but firm pressure is again applied as in the original fixation. These procedures are repeated daily or every other day for a week or two, depending upon how clean and dry the edges are and how the central area is "taking." By then the graft is losing its pinkish hue and taking on the color of the donor site. It will have shrunk to a variable extent and the mold soiled so that it will be discarded. There may be a slight elevation of the scar about the graft where it conformed to the mold and where scar has joined the graft and border of the defect. Fibrosis has, of course, occurred between the graft and its recipient bed, this tends to cause wrinkling of the graft as it undergoes its inevitable shrinking. To minimize the amount of shrinking and to keep the graft permanently flat, pressure must be maintained for at least three or four weeks. The grafts will usually have regained their donor site color by the fourth to fifth week and will often soften sufficiently at the end of six to eight weeks so that it can be determined whether any excision or readjustment of



Fig 5.—Similar case showing relief of ectropion of lips and hypertrophied scar in beard area with three separate Wolfe grafts from clavicular region.



Fig 6.



Fig 7

Fig 6.—Partial destruction of alae and eversion of lips due to burn.

Fig 7.—Outer alar scarred tissue was turned downward as a lining and entire dorsum of nose grafted. Edges of Wolfe grafts in lips may need revision.

the edges will be necessary. Patients should be told that edges of these grafts may be raised, thickened, or show stitch marks and that a relatively minor secondary surgical procedure will be necessary or, at least, advisable.

### COMPLICATIONS

Complications which may be noted at initial dressing and a method of treating them are as follows:

1. Blebs on the graft surface. These should be gently opened with a sharp blade, fluid expressed, and 20 per cent mercurochrome applied.

2. Separations at the suture line. These can be reapproximated and held in position with strips of flamed adhesive tape, about 1 by  $\frac{1}{8}$  inch, applied gently directly across the edge.

3. Hematomas under the graft. These usually are indicated by a circumscribed dark red area within the graft, with more or less bulging. If at the edge, it is evacuated by simple expression, reapproximating the edge with flamed adhesive. If the hematoma is not at the edge, it can be evacuated through a stab wound with a bayonet-pointed blade.

4. Serum under the graft. This complication is handled similarly to hematomas. Areas of serous accumulation are denoted by fluctuant bulges with a pale pink or slightly cyanotic hue. The graft is often viable in these areas and there is a good chance that, if the serum is evacuated, this skin may become attached and survive following reapplication of pressure.

5. Areas of necrosis. These, in our experience, are usually small and involve only the superficial portion of the graft. They appear as a demarcated blue or black area along an edge or within the graft. Nothing is to be gained by disturbing them as separation takes place between the eighth to twelfth day, when the superficial necrotic tissue can be dissected off with small scissors, leaving the viable deep surface of the graft; it has the appearance of a pinkish-mottled dermis, closely resembling a skin graft donor site. Our preferred application is a single-ply, fine mesh, scarlet red gauze, over which the usual pressure dressing is reapplied while dry epithelization ensues. This commonly requires at least one week, but sometimes two to four weeks.

Any of these complications can occur during the first two weeks and should be carefully scrutinized and patiently appraised and treated.

6. A remote, unpredictable and uncontrollable complication in some cases is pigmentation of the graft. Why this occurs more in some individuals and in fact, why it occurs at all is not explained so far as we know. We have noted it more often in dark-skinned individuals and it seems to be permanent. It may be possible that tattooing of these grafts to improve the color matching will be generally available in the near future. Thus far we have had no experience with it but are procuring the equipment for its trial.

### SUMMARY

A review of the technical considerations in Wolfe graft technique has been recorded. No claim is made for originality in any portion of this article. However, the utilitarian value and functional and cosmetic satisfaction of the Wolfe

graft have become more appreciated incidental to the innumerable indications for its use in definitive war surgery.

Since its limitations are so definite, the technique so exacting, and its success so dependent upon observation of the many fine considerations in its management, we feel that a record of observations in 100 or more cases may constitute a helpful guide to those who are interested in application and improvement of this type of graft.

Every step we have considered and each small point that has been discussed is, we believe, important. Omission of any one may cause loss of part or all of a graft, or at least a substandard or disappointing result. Observation of all of them will give the optimum chance for success and encourage greater use of the free full-thickness graft.

# RECURRENT PARATHYROID ADENOMA

## A CASE REPORT

LLOYD B. BURK, JR., M.D.,\* ANN ARBOR, MICH.

(From the Department of Surgery, University of Michigan Medical School)

MANY articles have been published on hyperparathyroidism. Its varied manifestations have been noted and great advance in the pathologic physiology has been made. This report concerns one more variation of the disease. It is believed that this is the first report of a case of recurrent parathyroid adenoma occurring in a glandular graft.

## CASE REPORT

L. R. L., a 31 year old white newspaper editor, first came to the University Hospital on March 3, 1943. He entered with a chief complaint of "sore knees." He had been in perfect health until one year prior to admission, at which time he experienced the insidious onset of aching in the knees. These symptoms were continuous and progressive in intensity. On the advice of his physician he had all of the upper teeth extracted, which failed to be effective in producing a remission. Eight months later the elbows became similarly affected. Four weeks before he came to this hospital he was pushing a car and quite suddenly had severe pain over the left tibial tubercle. Thereafter, flexion was markedly limited although he was not totally incapacitated. One week later, while walking, the left leg suddenly became very weak and he fell to the ground. The knee became quite swollen and he visited his physician, who aspirated bloody fluid from the knee joint. A roentgenogram of the

TABLE I. SUMMARY OF RENAL FUNCTION

	URINE	NPN* (MG. %)	BUN.† (MG. %)	UREA CLEARANCE		A RAY
				(1ST HR.)	(2ND HR.)	
1943	Loaded with w.b.c.	--	19	44%	31%	Parenchymal calcification
1945	Same	62.5	39.4	28%	23%	Same
1946	Same	51.3	--	71%	53%	Same

\*Nonprotein nitrogen.

†Blood urea nitrogen.

TABLE II. SUMMARY OF BLOOD CHEMISTRY

	CA (MG. %)	P (MG. %)	ALKALINE PHOSPHATASE*	ACID† PHOSPHATASE
1943				
Preoperative	158	40	19.5	6.3
Postoperative				
24 hours	8.1	3.5		
48 hours	10.1			
72 hours	10.5			
120 hours	9.0	3.0		
1945				
Preoperative	160	3.5	7.8	4.6
Postoperative				
24 hours	11.7	3.7		
48 hours	9.8	4.0		
72 hours	9.1			
10 months	9.6	2.8	2.6	3.4

\*Bodansky units

†King-Armstrong units.

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\*Trainee, National Cancer Institute



knee was made and the patient referred to an orthopedic surgeon. The latter diagnosed the disease correctly and referred him to this hospital.

Systemic review revealed occasional nausea, which the patient believed was due to "nervousness"; once or twice during a nine months' period he vomited. He had no urinary symptoms except for a slight increase in frequency. A twenty two pound weight loss had occurred in the eighteen months prior to admission. There had been no change in the size of the head as determined by hat size.



Fig 1.—Lateral skull roentgenogram showing prominence of the trabecular pattern due to demineralization of the bone

Past history was irrelevant as was the family history except for the death of his mother at the age of 53 years, four months following a goiter operation. The exact cause of death was not known.

Positive physical findings consisted of a very small, firm, nodular mass just to the left of the trachea and just at each tibial tubercle. There was a fusiform nontender mass in the condyles of both elbows.

X ray examination included a study of the skull, mandible, spine, pelvis, ribs, the long bones, and the knees. The significant findings were:

- (1) Prominence of the trabecular pattern and decalcification throughout the entire skeleton. This was especially pronounced in the skull (Fig. 1).
- (2) Small cysts in the tibial tubercles bilaterally. There was also a cystic area in the lateral condyle of the left femur. These are shown in Fig. 2.
- (3) Cystic lesions were present in the fourth, sixth, and seventh ribs on the right side and in the third rib on the left. Fractures were present through the cystic areas in the posterior axillary line of the sixth and seventh ribs on the right.
- (4) There was marked calcium deposition in the parenchyma of both kidneys. In Fig. 3 this calcification is demonstrated to good advantage as well as a large multilocular cyst in the right lumen.
- (5) The lamina dura about the teeth was absent.



Fig. 2—Anteroposterior and lateral views of the left knee demonstrating typical cystic changes of hyperparathyroidism in the tibial tubercle of the tibia and the lateral condyle of the femur.

**Significant Laboratory Findings**—The serum calcium was 15.8 mg per cent while the inorganic phosphorus was 4.0 mg per cent. Alkaline phosphatase was 195 Bodansky units and the acid phosphatase was 63 King Armstrong units. The urine was loaded with white blood cells. While there was moderate impairment of renal function by the urea clearance test (Table I), the blood urea nitrogen was within normal limits. The Sulkowitch test showed a four plus reaction for calcium excretion.

The diagnosis of hyperparathyroidism probably due to a parathyroid adenoma was apparent and on March 13, 1943, ten days after admission, operation was performed. A tumor mass measuring  $2\frac{1}{2}$  by 2 by 2 cm. was found in the position of the parathyroid beneath the lower pole of the left lobe of the thyroid. The mass was completely excised.



was 3.5 mg. per cent. Alkaline phosphatase was 7.8 Bodansky units and acid phosphatase was 46 King Armstrong units. The urinalysis was the same as on the previous admission; there was further impairment of renal function and the blood urea nitrogen was 39.4 mg. per cent.

X-ray examination revealed destructive lesions in both iliac bones. In the multilocular cysts there were areas which showed definite evidence of repair since 1943, while other areas showed progression in the extent of destruction. The flat plate of the abdomen showed the same extensive calcification. There was irregularity in the distal ends of both clavicles, possibly the results of bone destruction.

The diagnosis of a recurrent parathyroid adenoma producing hyperparathyroidism was made, and on March 16, 1945, operation was performed. At operation a firm gray tumor mass was found in the sternothyroid muscle. The mass was completely excised and was found to measure 2.5 by 2 by 1.5 cm.

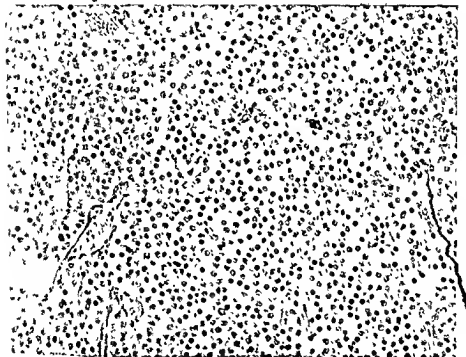


Fig. 1—Microscopic section of the primary adenoma of the parathyroid (X300)

Postoperatively the first day, the serum calcium dropped to 11.7 mg. per cent. The second day it was 9.8 mg. per cent and on the third day it was 9.1 mg. per cent. No intravenous calcium was given. The patient was placed on a high calcium diet with calcium supplements orally. No dihydrotachysterol was administered. He developed no definite signs of tetany but again had episodes of numbness of the arms and hands. He was discharged from the hospital on the fourth postoperative day with instructions to continue the high calcium intake.

The patient has reported that the paresthesia was present for ten days postoperatively and after that time did not recur. He was seen on Jan. 11, 1946, for checkup examination. At that time he was asymptomatic and there were no positive physical findings of significance. There was no evidence of a recurrent tumor in the neck and the blood chemistry findings were normal (Table II). The Sulkowitch test on the urine showed a two plus reaction for calcium. While renal function had apparently improved as evidenced by the urea clearance test (Table I), the nonprotein nitrogen in the blood was slightly elevated and the urine



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showed it to be loaded with white blood cells without the presence of organisms. He has been advised to have further urologic investigation.

X-ray examination showed complete recalcification of the skull and partial remineralization of the cervical spine. The cystic areas were nearly recalcified. In this regard the alkaline phosphatase was normal. A scout film of the abdomen revealed the tubular calcification to be unchanged, and, of course, it is extremely doubtful that this will ever significantly improve.

#### *Pathologic Report.*—

*Primary tumor:* The tumor mass measured  $2\frac{1}{2}$  by 2 by 2 cm. It was a large parathyroid adenoma showing areas of sclerosis and calcification. In a few areas there were eosinophilic cells and there were areas of old hemorrhage. Along one border there was a small amount of thyroid tissue. There was some indication that this adenoma may have penetrated its capsule. This is mentioned to call attention to the possibility of local recurrence (Fig. 4).

*Recurrence.* A large adenoma of the parathyroid was found in which there was variation of cell type, there being both small, dark chief cells and larger "ivoryshell" cells. Connective tissue trabeculae and many large blood spaces were found within the adenoma but there was no necrosis. There was abundant old hemorrhage, both within and surrounding the adenoma. The adenomatous tissue was not encapsulated, some of the lobules extending between bundles of striated muscle. Some of the cells of the adenoma were atypical in respect to shape and nuclear content. In general this recurrent adenoma was similar to that removed two years ago except that foci of eosinophilic cells were absent in this present specimen, and sclerosis was less marked (Figs. 5 and 6).

#### DISCUSSION

The clinical manifestations in both instances were typical of hyperparathyroidism and require no special comment. On the other hand, there are several pathologic aspects of this case which should be emphasized.

First of all, the capsule of the primary tumor had been penetrated and the possibility of recurrence suggested. This failed to occur at the site of the original tumor. Instead, recurrence apparently occurred as the result of proliferation of the transplant with a return of the manifestations of hyperparathyroidism.

Second, the original tumor was pathologically a parathyroid adenoma, which, of course, is no longer a medical oddity, it presented no characteristics of malignancy except for penetration of the capsule. On the other hand, in the recurrent tumor some of the cells were less typical, there was no encapsulation, and strands of cells were found between muscle bundles. The pathologists at the University Hospital are of the opinion that this tumor should not be diagnosed as carcinoma. While there are mild pleomorphic and hyperchromatic changes in some of the cells, the tumor is still of a well-differentiated type. The intermingling of tumor and muscle need not imply invasive growth since the transplant could not have had a limiting capsule on all sides.

#### SUMMARY

A case report is presented of a patient who had a parathyroid adenoma. At operation a fragment of the adenoma was transplanted between the strap muscles of the neck. Two years later the patient returned with a recurrence of all manifestations of hyperparathyroidism and a recurrent adenoma at the site of the graft. Pathologically, neither tumor was considered malignant.



wounds. The deep loop of the suture passes through the galea about 1 cm. from the edge and the superficial portion is through the cutaneous surface as near the free margins as possible (Fig. 2). In this manner skin and galea are acc-  
l and excellent healing is obtained (Fig 3).

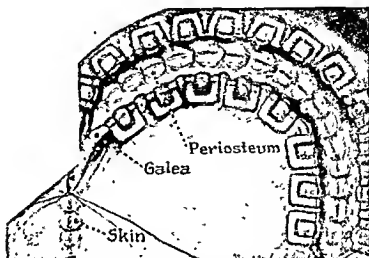


Fig 1—The usual two-layer technique of scalp suture with interrupted silk sutures in both galea and skin.

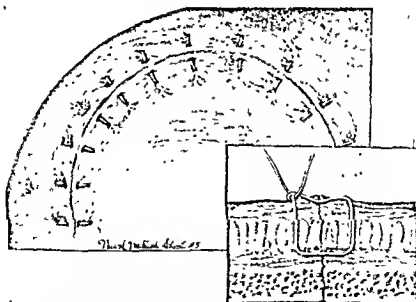


Fig 2—Accurate closure with single layer of tantalum wire mattress sutures.

It is desirable to leave the cut ends of the wire long enough so that they can be easily identified later, since the scalp reaction is so minimal that some may be overlooked in removing if the ends are cut too short.



## THE EFFECTS AND DRAWBACKS IN THE USE OF HEPARIN IN RETARDING MENSTRUUM

DAVID WEINER, M.D., AND KURT LANGF, M.D., NEW YORK, N. Y.

WITH THE TECHNICAL ASSISTANCE OF FLORENCE T. SCHIFFIN AND SOLOMON SNIDEN  
(From the Department of Medicine, New York Medical College, Flower and Fifth Avenue  
Hospitals, and the Metropolitan Hospital Research Unit)

THE use of anticoagulant therapy in the treatment and prevention of thrombo embolic diseases<sup>1,2,3,4</sup> as well as in the treatment of frostbite<sup>5,6</sup> is becoming more widespread as time passes. While dicumarol can be taken orally it has the distinct disadvantages of having a rather extensive time lag between administration and anticoagulant action and of offering considerable difficulties in predicting proper dosage in each individual case. These difficulties make it impossible to use the drug where an immediate and predictable effect on the clotting mechanism is desired.

Heparin, however, which does not have these disadvantages must be administered intravenously, preferably by intravenous drip, and its use is rather costly. It is, therefore, understandable that any method obviating these difficulties by the use of a retarding menstruum would be a distinct step forward. Loewen and his collaborators<sup>7</sup> have used heparin in Pitkin's menstruum subcutaneously in a series of rabbits and described satisfactory results. They describe even and prolonged elevations of the clotting time for long periods of time after one deposition of the preparation. Later, two of these authors<sup>8</sup> reported favorable results in fifteen cases of thrombophlebitis. Bryson and Code<sup>9</sup> obtained elevations of the clotting time for from seventeen to seventy hours in dogs by means of heparin in a beeswax mixture injected intramuscularly.

During the course of certain experiments on the prevention of gangrene subsequent to frostbite by the use of heparin, we found it necessary to search for a method by which heparin could be administered in single injections to experimental animals. The effect was supposed to be a long-lasting, predictable, and even elevation of the clotting time as one would desire it for use in patients. One hundred seventy-five rats and forty-five rabbits were used in the different phases of these experiments. Two preparations<sup>10</sup> were utilized in these experiments based on the suggestion of Loewen using heparin in Pitkin's menstruum. The composition of the two preparations, which differ only by way of the vasoconstrictor added to one of them, is shown in Table I.

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\*We are greatly indebted to Dr. W. T. Strauss of Roche-Organon, Inc., Roche Park Nutley, N. J., for supplying us with ample quantities of heparin in Pitkin's menstruum in its various forms.

TABLE I COMPOSITIONS OF LP 9 AND LP 10

	LP 9 (mg.)	LP 10 (mg.)
Crystallized sodium salt of heparin	100.0	100.0
Chlorbutanol	0.5	0.5
Eucapine dehydrochloride	1.0	1.0
Epinephrine hydrochloride	1.0	
Ephedrine sulfate	25.0	
Pitkin's menstruum (q.s. ad)	2.0 cc	2.0 cc

The addition of a vasoconstrictor to preparation LP 9 further contributes to the slow absorption of the heparin. Clotting times were determined by the Lee-White modification of Howell's method performed on heart blood in both rats and rabbits. The normal clotting time in rats by this method is between  $2\frac{1}{2}$  and 9 minutes; in the rabbit between 4 and 12 minutes.

A single subcutaneous deposition of 0.1 c.c. of the preparations LP 9 and LP 10 in rats results in a marked elevation of the clotting time for at least twelve hours, but of a rather uneven character. The beginning of the prolongation occurs considerably earlier with the preparation without vasoconstrictor than it does with the other. In general, it was our impression that preparation LP 10 (without vasoconstrictors) gives a more rapid effect but does not last so long as a deposition of LP 9 (with vasoconstrictors). None of the preparations produces an even prolongation of the clotting time during the period of its effectiveness (Table II).

TABLE II. AVERAGE CLOTTING TIMES OBTAINED IN FORTY RATS AT VARIOUS INTERVALS AFTER A SINGLE SUBCUTANEOUS INJECTION OF LP 9 AND LP 10

AMOUNT INJECTED	CLOTTING TIMES AFTER				
	2 HR.	4 HR.	8 HR.	12 HR.	24 HR.
0.1 cc. LP 9		Normal	Over 4 hr	45 min	Normal
0.1 cc. LP 10		Over 4 hr.	60 min	30 min	Normal
0.2 cc. LP 9	Normal	Over 24 hr.	Over 24 hr.	8 hr.	
0.2 cc. LP 10	Over 18 hr	12 hr	12 hr	12 hr	Normal

In order to obtain a rapid rise in clotting time as well as a prolonged action, both preparations should be injected at different sites since mixture of them in one deposition does not produce the desired effect (Table III).

While single injections produced a marked although not quite satisfactory response, because of the uneven characteristics of the curve of the clotting time, repeated injections in the same animal introduced serious complications. At the site of the second or subsequent depositions invariably huge hematomas formed as well in rats as in rabbits. Frequently these hematomas are so large that the animal actually dies from exsanguination. Many others showed definite signs of severe anemia. Of forty-nine rats receiving daily subcutaneous injections for five days, eighteen died spontaneously. All animals autopsied showed very large subcutaneous hematomas and signs of severe anemia and no other cause of death. The remaining thirty-one were sacrificed for various reasons. Of these, twenty-three were autopsied, nineteen showing large subcutaneous hematomas. These hematomas were occasionally so large that they trapped the heparin given in subsequent injections, causing an insufficient elevation of the clotting time.

TABLE III THE ACTION OF COMBINATIONS OF LP 9 AND LP 10 WHEN INJECTED IN THE SAME AND DIFFERENT SITES (SIXTEEN RATS)

AMOUNT INJECTED	CLOTTING TIMES AFTER	
	2 hr.	4 hr.
0.1 cc. LP 9 + 0.1 cc. LP 10 in same site	Normal	15 min
0.1 cc. LP 9 + 0.1 cc. LP 10 in dif- ferent sites	70 min	Over 2 hr

These difficulties, in so far as the rat is concerned, are largely avoided by injecting subcutaneously into the tail. Here the skin is firmly bound down to the subcutaneous tissues, effectively preventing the formation of large hematomas. Of fifty-one rats thus treated, only thirteen died and the remainder were adequately heparinized for the desired period of time.

The rats which died after injection into the tail, moreover, all died within one-half hour after injection, many with convulsions and gross bleeding from the nose and mouth. Autopsy on eleven of these showed multiple fresh pulmonary infarctions indicating that the Pitkin's menstruum had found its way directly into a vein. That this is a relatively infrequent accident is indicated by the fact that out of a total of more than 150 tail injections given it occurred only thirteen times. Gangrene of the tail frequently developed in rats thus treated due to interference with the circulation, but this does not interfere with the treatment if each injection is made proximal to the preceding one.

Forty-five rabbits were heparinized by the subcutaneous route using the preparations LP 9 and LP 10 combinations of both. All of them, as far as they were an opportunity to observe large hematomas at the site of the second and subsequent injections and many signs of a severe anemia.

In human beings hematomas probably occur at the site of injections indicated by intense pain lasting for many hours, but they are comparatively innocuous due to the different relation between the size of the hematoma and the total blood volume. Moreover it has been our experience that approximately 50 per cent more heparin is needed in human beings when given by subcutaneous deposition than by intravenous drip. However, patients who have already suffered blood loss, as well as anemic patients, should be watched carefully and transfusions given immediately if signs of further blood loss should appear.

#### SUMMARY AND CONCLUSIONS

1. The value of prolonged heparinization is discussed briefly and the literature on retarding menstrua reviewed.

2. Although the clotting times obtained after a single deposition of heparin in Pitkin's menstruum shows considerable spikes, a satisfactory elevation can be produced for twenty-four hours with 1 cc. of the experimental preparation.

3. In small animals repeated administration of Pitkin's menstruum leads to the formation of large hematomas and does not cause the death of the animal. In human beings repeated administration of Pitkin's menstruum leads to the formation of large hematomas and does not cause the death of the patient.

4 These difficulties are overcome in the rat by injection into the tail.

5 In human beings the small size of hematomas compared to the total blood volume probably renders them less important but great care should be exercised in anemic patients.

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## TANTALUM SCALP SUTURES

LIEUTENANT COMMANDER C. HUNTER SHILDEN, LIEUTENANT COMMANDER ROBERT H. PUDENZ, AND LIEUTENANT COLLIN S. MCCARTY, MEDICAL CORPS, U.S.N.R.

*(From the Neurosurgical Service, Department of Surgery, U. S. Naval Hospital, National Naval Medical Center, Bethesda, Md.)*

THE method of suturing the scalp has changed very little during the period of development of neurosurgery. The two-layer technique (Fig. 1), using silk in the galea and skin, has become universally accepted. Slight variations, such as continuous silk or dermal in the skin, have been advocated by some surgeons, but most have adhered to the principle of closing the scalp in two layers. Babcock popularized the use of stainless steel as a suture material. One has used for years a vertical mattress stitch of this material in closing craniotomy wounds. This method probably is employed by other surgeons.

The two-layer technique produces excellent wounds but does possess several disadvantages. A large amount of foreign material is buried in the scalp, adding a potential source of infection. Even without infection the sutures may produce a point of local irritation in the scalp and necessitate removal. It is not uncommon, even many months after operation, to have a patient complain of catching the teeth of a comb in an old suture that has worked to the surface.

The two-layer technique is a tedious procedure which consumes unnecessary time at the end of the operation when the general condition of the patient may be the cause of some concern. Furthermore, during the additional time of closure a far greater amount of blood is lost than is generally appreciated. Because of these factors, it seemed worth while to investigate other methods that were more rapid and did not leave buried suture material in the scalp.

It has been a common practice to use a single layer of interrupted heavy silk sutures for secondary closure of a craniotomy. This saved much time and produced satisfactory results. It seemed logical to adapt this procedure to the primary closure of scalp wounds. We used silk at first, but found that through-and-through sutures placed some distance from the scalp edge tended to evert the edges and did not produce the desired fine line of healing. If this method of suture were converted into a mattress type, returning through the scalp a few millimeters from the margins, accurate approximation was obtained but reaction and often minute stitch infection occurred. These features were objectionable, and the method was not used routinely even though mechanically satisfactory.

The introduction of tantalum afforded a material which produced no tissue reaction.<sup>1,2</sup> It is used extensively as a nerve suture material and should be equally effective in the scalp. During the past year interrupted mattress sutures of fine tantalum wire (0007) have been used to close all craniotomy

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wounds. The deep loop of the suture passes through the galea about 1 cm. from the edge and the superficial portion is through the cutaneous surface as near the free margins as possible (Fig 2). In this manner skin and galea are accurately approximated and excellent healing is obtained (Fig. 3).

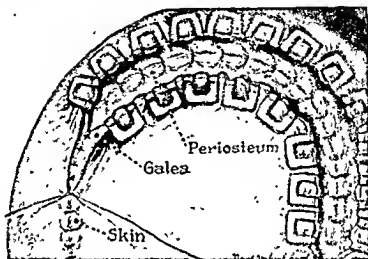


Fig 1—The usual two-layer technique of scalp suture with interrupted silk sutures in both galea and skin.

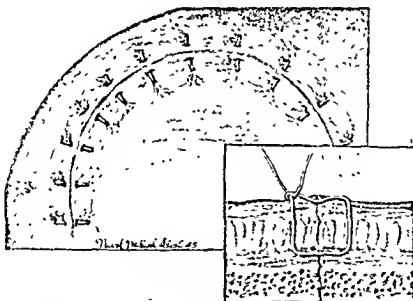


Fig 2—Accurate closure with single layer of tantalum wire mattress sutures.

It is desirable to leave the cut ends of the wire long enough so that they can be easily identified later, since the scalp reaction is so minimal that some may be overlooked in removing if the ends are cut too short.

An added feature is the fixation of the dressing. The gauze mesh is held by the cut ends of the wire so that the gauze placed directly on the suture line is accurately held, thus preventing the dressing from sliding back and forth. This may be as important as the application of wound towels during the operation.

The wire sutures are easily removed without discomfort to the patient and the ultimate result is a well-healed wound which contains no foreign material (Fig. 4).



Fig. 3

Fig. 3—Tantalum wire sutures ten days after operation. There is minimal reaction about the sutures and excellent approximation of wound edges.



Fig. 4

Fig. 4—Photograph of healed craniotomy incision. All foreign material is removed from the scalp.

This method should be well suited to the primary closure of traumatic scalp lacerations. It affords an easier and more rapid method of closure with a minimum loss of blood.

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## A NEW SUCTION TUBE FOR CHEST AND ABDOMINAL OPERATIONS

FRANK CARROLL, M.D., SAN FRANCISCO, CALIF.

(From the Department of Surgery, Stanford University School of Medicine)

FOR a number of years a modification of the Pool abdominal suction tube has been in use on the surgical clinic service at Stanford University Hospital. It was primarily designed for operations within the chest, but it is equally useful in abdominal procedures.

The new tube is interchangeable with the conventional Pool tube so that either one may be used during an operation without disconnecting the suction. The cap is eccentrically placed so that suction may be used on the sides of the chest or abdominal wall, as well as on the bottom of the cavity. The cap is also detachable, which facilitates cleaning.

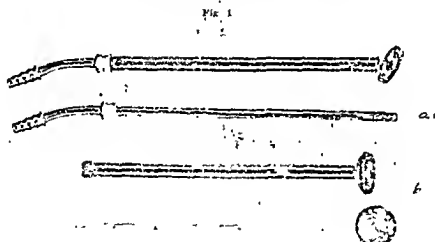


Fig. 1—The assembled tube.

Fig. 2—A Pool tube with a new tube attached to its cap.

The new tube\* has the advantage of the suction being applied to the end of the instrument rather than along the sides, as in the Pool tube. This permits the complete aspiration of pockets of blood and exudate. Clots and fibrin can be removed with ease from the smooth surfaces of the abdominal and chest walls. Whenever possible, suction is used instead of sponging thereby lessening the amount of trauma, with resultant prevention of adhesions.

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\*The tube may be obtained from A. Mueller & Company, 405 South Hill Street, Chicago, Ill.



# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## INTESTINAL OBSTRUCTION DUE TO PERFORATIONS OF THE GALL BLADDER

AN ANALYSIS OF FORTY-ONE CASES OF PERFORATED GALL BLADDER IN ELEVEN OF WHICH THERE WAS ASSOCIATED INTESTINAL OBSTRUCTION

ALEXANDER BLAIN, III, M.D., AND HENRY N. HARKINS, M.D., BALTIMORE, MD.  
(From the Departments of Surgery and Pathology, Johns Hopkins University Medical School and the Johns Hopkins Hospital)

GALLSTONE ileus, the result of perforations of the gall bladder into the intestinal tract, has received much attention in the literature. We have been able to find nothing in the literature which draws attention to the relation of other types of gall bladder perforation to intestinal obstruction. Since in this present study, perforations of the gall bladder without fistula formation have resulted in over one-half of the intestinal obstructions in our total series, it is thought worth while to draw specific attention to the inflammatory results of gall bladder perforation as a cause of intestinal obstruction.

The surgical records for the past twenty years (1926 to 1945) and all the autopsy records since the opening of this hospital (1889 to 1945), a period of fifty-five years, have been searched for cases of perforation of the gall bladder. Forty-one cases were found, exclusive of those on a traumatic basis. These cases have been divided according to Niemeier's classification into three groups:

- Type I (Acute free perforation into the peritoneal cavity), 13 cases
- Type II (Subacute perforation with pericholecystic abscess), 15 cases
- Type III (Perforation into a viscus), 13 cases

Of the eleven cases in this series in which intestinal obstruction was an associated factor five patients (33 per cent) were seen with type I perforations, one (7 per cent) with type II perforations, and five (38 per cent) with type III perforations.

In the last group the five cases of obstruction were due to the extrusion of gallstones into the intestinal tract with resultant "gallstone ileus." The other eight cases of type III perforation, although associated with cholecystenteric fistulas, did not result in gallstone obstruction. The obstructions associated with the other types of gall bladder perforation either were paralytic in nature due to generalized peritonitis or were due to pressure of the perforating gallstone into the intestinal tract by an inflammatory mass. The fact that the obstruction was the

obstructive symptoms either overshadowed the symptoms of cholecystitis with perforation or confused the diagnosis made us decide to put this analysis of our cases on record.

#### GENERAL CONSIDERATIONS

*Incidence of Gall Bladder Perforations.*—Our series of forty-one perforations of the gall bladder represents all those available in the surgical records of the Johns Hopkins Hospital for the twenty-year period, January, 1926, to January, 1945, plus all the autopsy material from 1889 to January, 1945 (a period of fifty-five years). During the periods stated there were 11,794 gall bladder operations in which the incidence of perforation was 0.3 per cent (twenty-nine cases) and there were 19,274 autopsies in which the incidence of gall bladder perforation was 0.01 per cent (seventeen cases). Twelve of the cases in this series were counted under both headings. All of the 735 gall bladder operations at this hospital from 1889 to 1924 have been analyzed by Blalock (1924). In this group there was one cholecystenteric fistula and there were nineteen cases of peritonitis due to gall bladder disease.

Cowley and Harkins (1943) found an average incidence of 2.6 per cent perforations in 12,915 reported operations on the gall bladder. The lowest incidence of perforation (0.9 per cent) was in their series of twenty-five cases reported at Henry Ford Hospital. The highest incidence, 12.1 per cent, was reported by Mentzer (1936). On the other hand, when only cases of acute cholecystitis are considered, the incidence is higher. Cowley and Harkins (1943) reported an average incidence of 13.0 per cent in a collected series of 2,261 cases of acute cholecystitis. Hicken and Coray (1943) reported that their twenty-four cases of gall bladder perforation represent "25.6 per cent of all the 'acute gall bladders' operated upon."

*Mortality From Free Perforations of the Gall Bladder.*—In the group of nine patients operated upon (Tables I, II, and III) there were five deaths (55 per cent mortality). In this group, two cases (Cases 3 and 5) were diagnosed correctly and the patients underwent cholecystectomy. One of these died on the second postoperative day of a cerebral vascular accident associated with a complete right hemiplegia. The other died on the fourth postoperative day with what proved to be at autopsy a rupture of the left ventricle. Another patient

TABLE I. MORTALITY OF SURGICAL CASES OF FREE AND LOCALIZED FREE PERFORATIONS OF THE GALL BLADDER

AUTHOR	FREE PERFORATIONS		LOCALIZED PERFORATIONS	
	NUMBER OF CASES	PERCENTAGE MORTALITY	NUMBER OF CASES	PERCENTAGE MORTALITY
Siemsen (1914)	2	0	6	0
Sanderson (1917)	4	50	42	14
Leahy (1928)	2	100	—	—
Stone and Thompson (1929)	6	0	11	9
Holt (1932)	53	26	17	0
Allen and Allen (1941)	4	50	11	9
Cowley and Harkins (1943)	2	67	22	5
Stamm (1942)	14	63	6	53
Cowley and Harkins (1943)	6	17	14	17
Chandler and Allen (1943)	9	55	20	15
Total of series	108	42	172	17

TABLE II NIEMEN TYPE I PERFORATIONS

NO	TYPE OF PERFORATION	AGE, SEX, AND RACE	PREOPERATIVE DIAGNOSIS	OPERATION
1	Generalized bile peritonitis	37, W., F.	Acute pancreatitis	Supra Exploratory laparotomy, cholecystectomy, and drainage of peritoneal cavity
2	Generalized purulent and bile peritonitis	40, W., F.	Acute exacerbation of chronic cholecystitis with lithiasis; no mention of perforation	Drainage of peritoneal cavity (cholecystectomy)
3	Generalized purulent peritonitis	74, W., F.	Perforation of gall bladder	Cholecystectomy
4	Generalized bile peritonitis	46, W., M.	Acute exacerbation of chronic cholecystitis with cholelithiasis, paralytic ileus	Drainage of gall bladder + stones; gallstones and bile general peritoneal cavity
5	Generalized bile peritonitis	67, W., M.	Acute cholecystitis with perforation resulting in generalized peritonitis	Cholecystectomy and drainage
6	Acute cholecystitis; localized abscess which had ruptured with generalized peritonitis and multiple abscesses of the pelvis	64, W., M.	Partial intestinal obstruction and acute abdominal condition	Exploratory laparotomy + drainage of abscess in right inguinal region; later, enterotomy was made for intestinal obstruction
7	Generalized bile and purulent peritonitis; abscesses drained off by omentum and transverse colon	77, W., F.	Acute pyelonephritis and acute cholecystitis with cholelithiasis	Cholecystectomy with drainage (exploratory laparotomy over palpable mass)
8	Type I Acute free perforation with rupture of bile down into the gut	47, W., M.	Intestinal obstruction due to inflammatory or neoplastic cecal mass (acute complete)	Exploratory laparotomy + manual ileostomy for partial ileocecal obstruction
9	Acute free perforation	77, W., F.	Acute appendicitis (retrocecal?)	Cholecystectomy with drainage
10	Generalized purulent and bile peritonitis	7, F.	Typhoid fever (1901)	No operation Autopsy

ACUTE FREE PERITONITIS

RESULT	STONES	BACTERIOLOGY	PATHOLOGY
<i>Cases</i>			
Well	-	<i>Staph aureus</i> hemolyticus	Fragile ruptured gall bladder removed at operation
Well	+	Gall bladder, no growth in 72 hr	Ruptured gall bladder drained but not removed
Died (ruptured heart), (autopsy)	+	Gall bladder and general peritoneal cavity, <i>Fach coli</i> (heavy growth), and gamma str (light growth)	Cholelithiasis, ulcerative cholecystitis with thrombosed arteries and veins in wall of gall bladder
Well (returned one year later with symptoms, refused to be admitted)	+	In stoneal cavity, no growth on blood agar or in broth	Ruptured gall bladder drained but not removed
Died (cardio-vascular accident), (no autopsy)	+	Gall bladder, alpha str., peritoneal cavity, light growth of gamma str	Chronic ulcerative cholecystitis with perforation and abscesses several in size in wall of gall bladder, infiltrated with PMNs
Died (autopsy)	Mass of inspissated bile	Cultures of atoxenic <i>B coli</i>	Acute cholecystitis, rupture of gall bladder with abscess in large intestine out of right mesocolon and many small abscesses in cecal region, no acute chronic adhesions, peritonitis, catarrh of stomach
Died (no autopsy)	+	Pocket of turbid bile in abdomen, <i>B coli</i> (heavy growth), urine, <i>B coli</i> (heavy growth)	Ruptured gall bladder drained but not removed
Died (autopsy)	+	4+ blood smear, no organisms seen, culture, <i>Fach coli</i> (over 1000 colonies on original plate) peritoneum smear, no organisms, culture proteins, <i>Fach coli</i> and gamma str fecalis	Chronic cholecystitis and cholelithiasis with abscess in wall of gall bladder which had burrowed through the wall dissecting the liver, and finally perforated with leakage of bile down the cholelith gutter
Well	+		Cholelithiasis, chronic ulcerated cholecystitis, there is an area of necrosis in the gall bladder 2.5 cm. below fundus, in the area of the necrosis there is a perforation
<i>(Patients Not Operated Upon)</i>			
Died (autopsy)	+		Typhoid fever with hyperplasia and ulceration of Peyer's patches, hyperplasia of mesenteric lymph nodes, cholelithiasis and cholecystitis with perforation of the gall bladder and generalized peritonitis; no intestinal perforation

(Table II continued on following pages.)

NO	TYPE OF PERFORATION	AGE, RACE, AND SEX	PREOPERATIVE DIAGNOSIS	OPERATION
11	Free perforation at first confined to lesser peritoneal sac and then generalized peritonitis	♀	Died Oct. 11, 1898, and autopsy done by Dr. Flexner; paralytic ileus	No operation (1)
12	Generalized bile and purulent peritonitis and also large pericholecystic abscess	70, W, M.	1 Carcinoma of colon with metastases to liver and lungs 2 Carcinoma of stomach	No operation
13	Generalized purulent peritonitis	73, W, F.	Acute cholecystitis and cholelithiasis; generalized peritonitis; paralytic ileus	Refused operation

(Case 1), died the day after cholecystostomy. Prior to death there was a temperature of  $105^{\circ}$  F. associated with marked respiratory distress. No autopsy was obtained. Two deaths were due to the lack of a correct diagnosis.

The first of these patients (Case 8) was found at operation to have an inflammatory mass producing complete obstruction in the region of the cecum. An ileostomy was performed. The patient died and at autopsy was found to have a perforated gall bladder. Gall bladder contents had escaped down the paracolic gutter to produce the inflammatory paracecal mass. Our interest in this case resulted in this study of perforated gall bladders to determine the incidence and mechanism of associated intestinal obstructions.

The second patient (Case 6) had an exploratory laparotomy for an acute abdominal condition associated with partial intestinal obstruction. A right inguinal abscess was drained. Autopsy revealed a perforated gall bladder which had given rise to the abscesses and intestinal obstructions in each of these cases.

In the group of four cases in which operation had not been done and in which the perforation was discovered at autopsy, two of the deaths (Cases 10 and 11) were in patients (in 1898 and 1901) whose clinical records are not available. One was associated with typhoid fever; neither was operated upon. One death (Case 12) was attributable to the fact that the patient entered the hospital highly jaundiced and moribund. The clinical impression was that the patient had carcinoma of the colon with metastases to the liver and lungs. The second most likely possibility was considered to be a carcinoma of the stomach. Autopsy revealed a carcinoma of the common bile duct at the ampulla of Vater producing partial high intestinal obstruction and chronic cholecystitis with abscess formation in the anterior wall of the gall bladder. The gall bladder had per-

CONT'D

RESULT	STONES	BACTERIOLOGY	PATHOLOGY
ied (autopsy)	+	Peritoneal cavity, abscess, liver, Friedlander bacillus	Greatly thickened and inflamed gall bladder full of pus as were all its dilated ducts. It had perforated into an abscess cavity posteriorly (caused by perforation). One stone in gall bladder and two in abscess in lesser omentum. Perforation of abscess with generalized peritonitis and paralytic ileus; viscera covered with fibrinous adhesions.
ied (autopsy)		Heart blood <i>Esch coli</i> ; peritoneal fluid, <i>Esch coli</i> ; or, 50 col and pneumococcus, type 7, 25 col.	Carcinoma of common duct of ampulla of Vater with marked dilatation of pancreatic and bile ducts, jaundice, chronic cholecystitis and abscess formation in anterior wall of gall bladder with perforation into lesser omentum, biliary fistula and abscess, as and abscess in liver, perforation into lesser omentum, morbid away from it.
ied (autopsy)	+		Cholelithiasis with impaction of one stone in common duct near papilla, obstruction and dilatation of common duct, jaundice, ulcerative cholecystitis with perforation of wall, local and general edema of fibrinous purulent peritonitis.

perforated into the peritoneal cavity with resultant peritonitis. The site of the perforation was not near the tumor. There was associated cholangitis and biliary cirrhosis. The fourth patient in this group (Case 13), although having an essentially correct diagnosis, refused operation.

The mortality percentage of 35 in the new patients operated upon is slightly higher than the average and is considerably higher than such figures as those of Niemeier (0 per cent), Stone and Douglas (0 per cent), Hettr (35.9 per cent), and Cowley and Harkins (16.6 per cent). It should be pointed out that our series includes patients treated almost fifty years ago. Four additional deaths were in patients upon whom no operation was performed. Failure to recognize the correct pathologic process underlying the picture of intestinal obstruction was responsible for two of the deaths.

**Mortality From Localized Perforations of the Gall Bladder.**—In the group of twelve Niemeier type II perforations (with localized pericholecystic abscess) treated by operation, there were no deaths (0 per cent mortality) as shown in Tables IV and V. Three other nonoperated cases were found at autopsy. In

TABLE III. NIEMEIER TYPE I (WHITE FLEE) PERFORATIONS. SUMMARY

Surgical patients reviewed	4
Surgical patients dead	5
Total surgical cases	9
(37 per cent mortality)	
Autopsy cases (1 patient not operated upon)	4
Total cases	13
Cases with intestinal obstruction*	5

TABLE IV. NIEMEIER TYPE I

N. N. AGE	TYPE OF PESTERATION	AGE, SEX, AND SEX	PREOPERATIVE DIAGNOSIS	OPERATION
14	Localized abscess	20, W. M.	Rupture of gall bladder	Cholecystectomy <i>Sargent</i>
15	Localized abscess	37, N. F.	Subsiding attack of acute cholecystitis superimposed on cholelithiasis	Cholecystectomy
16	Localized abscess with colic, on or just above dome of liver	70, W. M.	Acute abdominal emergency, etiology unknown	Exploratory laparotomy; cholecystectomy and drainage
17	Localized abscess at 1/2 and pushed between stomach and duodenum	50, W. M.	Acute abdominal emergency 1. Acute cholecystitis 2. Acute pancreatitis 3. Perforated ulcer; peritonitis	Exploratory laparotomy and drainage of abscess
18	Localized abscess	5, N. F.	Acute exacerbation of chronic cholecystitis with cholelithiasis	Cholecystectomy
19	Localized abscess	61, W. F.	Acute cholecystitis with cholelithiasis, possible empyema of gall bladder	Cholecystectomy
20	Localized abscess	60, W. F.	Chronic cholecystitis and cholelithiasis	Excision, cholecystectomy, appendectomy
21	Localized abscess	33, W. F.	Acute cholecystitis and empyema of gall bladder	Cholecystectomy
22	Localized abscess (extra-peritoneal cavity), tension	32, N. M.	Common duct stone and ascending cholangitis	Cholecystectomy

PERFORATIONS (PERICHOLECYSTIC ABSCESS)

RESULT	STONES	BACTERIOLOGY	PATHOLOGY
Cases			
Well	+		Ruptured gall bladder drained but not removed at operation a gangrenous area with a hole 1 cm long was found, there was a localized abscess containing 10 cc of pus about perforation
Well	+	<i>B. coli</i> (heavy growth)	Emphysema of gall bladder rupture with formation of a localized abscess covered by omentum; ruptured gall bladder drained but not removed
Well	+	Gall bladder, <i>Esch. coli</i> , abdominal cavity, <i>Esch. coli</i> (about liver)	Gall bladder wall thick and hemorrhagic, mucosa ulcerated and covered with a fibrinopurulent exudate; the wall was infiltrated with PMNs and was scarred there were areas of necrosis. Final diagnosis: cholecystitis with ulcerative cholecystitis with perforation
Well	None found	Abscess, <i>B. coli</i> (heavy growth)	Ruptured gall bladder drained but not removed about a quart of bile escaped into the space between stomach and diaphragm (walled off by omentum), gall bladder thickened and grayish white in color, perforation at junction near junction with cystic duct
Well	+	Culture of abscess, no growth	Gall bladder contained large stone 3 cm in diameter and was neutroly inflamed; its fundus was necrotic and had perforated into an abscess cavity between gall bladder and anterior abdominal wall, abscess well localized by omentum and contained 20 cc of bile stained fluid
Well	+	Gall bladder, <i>B. coli</i> (heavy growth)	Omentum adherent to gall bladder and between them a pocket of pus, acute gangrenous cholecystitis with perforation at ampulla, emphysema of abdominal wall
Well	+	Culture of abscess, sterile, readmitted 2 months later with severe intestinal obstruction due to adhesions, relieved completely with gastrostomy	Thickened gall bladder wall with invasion of mucosa, hemorrhage, PMNs and giant cells in wall, subsequent organization chronic cholecystitis and cholecystitis with perforation about one centimeter from neck to fundus between gall bladder and anterior abdominal wall, pus under the liver, emphysema of gall bladder
Well	+	Culture of abscess, <i>B. coli</i>	Ruptured gall bladder drained but not removed, it was entirely encapsulated by omentum. Between the two abscesses considerable amount of bile stained pus. Gall bladder collapsed and it communicated with abscess via perforation. It contained pus and small stones cholecystitis. On a later admission, specimen showed chronic cholecystitis
Well	+	Extraluminal stones causing pressure on common duct	Gall bladder had ruptured at ampulla, extra-peritoneally, discharging stones, one of the stones impinging on common duct and responsible for jaundice; no stone in common duct but stones in cystic duct; gall bladder tense and showed marked chronic ulcerative cholecystitis

Table IV continued on following page



No.	TYPE OF PERFORATION	AGE, FACT, AND SEX	POSTOPERATIVE LESIONS	OPERATION
1	Type II. Localized abscess containing bile (almost type I if appendicitis a direct result)	41, N, M.	Acute cholecystitis with perforation and generalized peritonitis; peridiverticular perforation of intestine and mass in gall bladder region; acute cholecystitis	Cholecystectomy
2	Localized pericholecystic abscess	39, N, M.	Carcinoma of stomach	Exploratory laparotomy; cholecystectomy; 5 days age
3	Localized abscess	51, N, F.	Acute cholecystitis and cholelithiasis; no mention of rupture	Cholecystectomy
4	Localized abscess with localized fibrinopurulent peritonitis	65, N, F.	Carcinoma of gall bladder. In foetal hydronephrosis; heart failure, renal insufficiency, cardiovascular accident	No operation
5	Localized pericholecystic abscess, still containing gall stones	43, N, F.	Cardiovascular renal disease with hypertension; myocardial insufficiency, terminal pneumonia	No operation
6	Localized pericholecystic abscess	65, W, M.	Benign prostatic hypertrophy; chronic pyelonephritis, bilateral insufficiency	No operation

the group of eight Numerer type III perforations (six of them at laparotomy treated by operation, there were three deaths (37.5 per cent) (Table I). The other non-operated cases were found at autopsy. Thus, of the perforations, surgical cases with localized perforation of the gall bladder, the mortality after operative attack, a mortality of 15 per cent. (15 of 100 cases) is the average in the collected series shown in Table I.

*Incidence of Gallstones as Etiology of Intestinal Perforation.*—In 14 cases of intestinal obstruction due to perforation of the gall bladder, 12 per cent of all the gallbladder perforations (12 of 100 cases) were the cause of intestinal obstruction. Of all the specimens, a total primary (Table I) perforation of the gall bladder

-CONT'D

RESULT	STONES	BACTERIOLOGY	PATHOLOGY
Tell	Mass of inspissated bile	Gall bladder, heavy growth of <i>E. coli</i>	Gall bladder almost completely gangrenous and surrounded by a pocket of bile walled off by stomach, colon, and liver; it was tense and contained 40 cc of thick, dark, fecal smelling bile. Most of the mucosa had disappeared and necrosis extended all the way through the wall which was heavily infiltrated with PMNs and round cells.
Tell	Piece of black putty like material	Abscess, <i>Esch. communior</i>	Fresh fibrinous peritoneal adhesions walled off an abscess about gall bladder, containing 400 cc of bile stained pus; abscess communicated with lumen of gall bladder through necrotic perforation in fundus about 2 cm in diameter; ruptured gall bladder drained, but not removed.
Tell	+	Abscess, gamma str. fecalis	Gall bladder found covered by stomach and between the two was an abscess containing 3 cc of thick yellow pus; abscess communicated with a perforation in gall bladder. Final diagnosis: Cholelithiasis, ulcerative cholecystitis with perforation.
Patients Not Operated Upon)			
led (autopsy)	+	Abscess, <i>Esch. coli</i> (1000 col on original plate) and <i>Cl. welchii</i> , blood culture, <i>Esch. coli</i> and <i>B. subtilis</i>	Chronic cholecystitis, cholelithiasis, stone in ampulla of Vater, dilatation of bile ducts, acute hepatitis, empyema of gall bladder, adhesion to colon, stomach, duodenum, a rupture of the duct and abscess about right lobe of liver, localized fibrinopurulent peritonitis, nephritis.
led (autopsy)	+		An incidental finding at autopsy was cholecystitis and cholelithiasis with several large gallstones outside of gall bladder between gall bladder and liver partly eroding liver, perforation was sealed over and the extrahepatic stones were well walled off.
led (autopsy)	None mentioned		Ulcerative diphtheritic cholecystitis with perforation, abscess in wall of gall bladder and liver, gall bladder distended with bile; mucosa contains many yellow ringed necrotic areas, one of which was perforated, forming an abscess under the neck of the gall bladder near superior part of the duodenum; carcinoma of prostate, cystitis, pyelonephritis, pneumonia.

Recent of modern surgical methods the frequency of this condition has diminished. There have been numerous reports of isolated cases since Bartholin reported the first case in 1661. Courvoisier collected 151 instances of the syndrome in 1890 and Moore (1913) estimated that about 300 cases had accumulated in the literature by 1912. Fisher (1858) noted the prevalence of obstructions due to gall stones as 7.7 per cent. Leichtenstern (1876) rated it as 3.6 per cent of all cases of stone in series of collected cases in the early literature, but subsequent reports have put the figure between 0.36 and 2.2 per cent.

**Complications Associated With Internal Biliary Fistulas.**—As already stated, of the 104 patients treated by operation, three died, a mortality of 2.8 per cent.

TABLE V. NINETEEN TOTAL HEPATECTOMY FOR PRIMARY BILIARY CALCULI. SUMMARY

Surgical patients (ten treated)	12
Surgical patients (died)	0
Total surgical cases	12
(0 per cent mortality)	
Autopsy cases (patients not operated upon)	7
Total cases	19
Cases with intestinal obstruction*	1
*Seven per cent with intestinal obstruction	

Eight of the entire group of thirteen internal fistulas were unassociated with gallstone obstruction as shown in Tables VI and VII. Two of these fistulas contained large gallstones which had not entered the intestinal tract sufficiently to produce obstruction. In one case the fistula was due to a carcinoma of the gall bladder from which the patient died. Two others also had carcinomas of the gall bladder, but the fistulas in these it appeared that the perforations into the intestine were not due to the existing carcinomas but to the pressure necrosis not far produced by the stones. Of the eight cases unassociated with gallstone obstruction six patients died (five without operation). Three of these deaths were due to carcinoma of the gall bladder. Two of the fistulas were incidental findings at autopsy in patients dying of tuberculous meningitis and septicaemia, respectively. It is interesting that the remaining death was in the first patient ever autopsied at this hospital. He was a 68-year-old white male who is said to have been under Dr. Osier's service in 1889. He was intensely jaundiced, obstructed, emaciated, and moribund on admission. Autopsy revealed chronic cholecystitis and cholangitis, a common duodeno-duodenal fistula and gall stones (as only the gross report available). There were two other fistulas of the kind in this study. One was due to tuberculous ulceration of the duodenum and the other was not a true fistula but functioned as such. This case was one in which there was marked dilatation of the common bile duct associated with a congenital stenosis of the duodenum. A case of rupture and incision of the gall bladder by a duodenal ulcer was also encountered but has not been included in this report.

*Mortality From Gallstone Heur.* Of 133 patients with internal biliary disease seen at the Mayo Clinic and reported by Judd and Burden (1925) only one died of obstruction of the intestine by a gallstone. In institutions such as the Johns Hopkins Hospital located in a large community, however, this low incidence of associated obstruction is not to be found. The factor of gallstone obstruction was present in over one third of the fistulas seen and in over one-half of the fistulas coming to operation (five out of eight cases). Two of the five patients with gallstone thus died (a mortality of 40 per cent). One died while on the operating table as the primary incision was being made. This death was justifiably attributed to spinal anesthesia. No autopsy was obtained. The second patient died on the second postoperative day following an exploratory laparotomy for what was believed to be "carcinoma of the gall bladder with

pressure on the duodenum causing high intestinal obstruction." A carcinoma of the gall bladder which was invading the liver was found at operation along with cholecystitis and cholelithiasis with a cholecystoileal fistula. The fistula was not directly associated with the carcinoma. Autopsy revealed that the immediate cause of death was complete intestinal obstruction due to a large gallstone which had lodged in the terminal ileum.

Our mortality rate of 40 per cent for gallstone ileus is similar to that cited by other authors (50 to 80 per cent as reported by Martin, 1912, Powers, 1928, Vick, 1932, Vidgoff, 1933, Borman and Rigler, 1937, Balch, 1938; and in a discussion in the *Proceedings of the Section on Surgery of the British Medical Association* in 1925). On the other hand, the mortality of intestinal obstruction due to all causes was reported as 26.6 per cent by Vick (1932). Since the advent of duodenal suction and Miller-Abbott tube drainage, this mortality due to all types of obstruction has diminished to from 15 (Lough, Nelson and Swenson, 1940, and Dennis and Brown, 1942) to 22 per cent or less (Lewis, Shapiro and Vaughan, 1940, and Schlieke, Bergen, and Dixon, 1946). Johnston (1946) reported a mortality of 19.1 per cent in sixty-three patients at the Denver Receiving Hospital with nonstrangulated obstructions.

The high mortality from gallstone ileus is not to be accepted as inevitable and the important contribution of Rigler, Borman, and Noble (1941) on the roentgen diagnosis of internal biliary fistula and gallstone ileus should materially in reducing it. Finney (1942) in discussing three cases of gallstone ileus reported at the Woman's Hospital in Baltimore mentions an instance in which a flat plate of the abdomen revealed the common duet and the hepatic duet outlined with air and also a suspicious shadow in the ileum. A diagnosis of gallstone ileus was made and the gallstone was removed. Two days later the patient again developed signs of obstruction and a second flat plate showed another gallstone in the lower ileum. A second operation was performed, and the gallstone was removed. That patient lived, but two of the other two patients died (a mortality of 33.3 per cent in the three cases, which Finney considered high). It is well known that the relatively high mortality due to gallstone obstruction is accounted for in part by the advanced age of the majority of patients and in part by the atypical clinical picture which makes a correct diagnosis difficult. The various features of this unusual but highly dangerous type of intestinal obstruction have been dealt with in great detail by others and it is not the purpose of this report to repeat them. It is always worth while to reiterate, however, that to be diagnosed the condition has to be thought of, especially when a surgeon is confronted with a case of intestinal obstruction in a patient over 50 years of age with a history of right upper quadrant pain or other symptoms referable to the gall bladder in whom no other cause for the obstruction is evident.

Although all five cases of gallstone obstruction had what would be classed as simple nonstrangulated obstruction, it is known that gallstones in the intestinal tract may be associated with volvulus (closed loop) above the site of the obstruction (Rosen, 1904; Smith, 1925), with strangulation of the bowel by overdistention (Storck, 1939), or with perforation leading to peritonitis (Balch,

TABLE VI NIEMEIER TYPE III

No.	TYPE OF PERFORATION	AGE, RACE, AND SEX	PREOPERATIVE DIAGNOSIS	OPERATION
1	Fistula into duodenum	64, W, M.	Pericious anemia in remis- sion; cholelithiasis with stones in common duct	<i>Surgical</i> Exploratory laparotomy
2	Fistula into colon	59, W, M.	Chronic cholecystitis and cholelithiasis	Exploratory laparotomy; re- lease of adhesions be- tween colon and small in- testine, cholecystectomy, exploration of common duct
3	Fistula of gall bladder into ileum associated with car- cinoma of gall bladder and gallstone ileus (carcinoma at one end of gall bladder, fistula at other)	63, W, F.	1 Carcinoma of gall bladder with pressure on duodenum causing high intestinal ob- struction 2 Hydrops of gall bladder, carcinoma of stomach with metastases to liver	Exploratory laparotomy
4	Fistula into stomach with gallstone ileus (1943)	49, W, F.	1 Paralytic ileus with chole- lithiasis 2 High intestinal obstruction and possible gall bladder disease	Exploratory laparotomy, re- moval of gallstone from terminal ileum
5	Fistula into small intestine	58, W, F.	Episode of high intestinal ob- struction "mesenteric in- type" Medical con- sultant. No obstruction at present, carcinoma with partial obstruction? Col- ostomy Diverticula? No op- eration indicated at present	Exploratory laparotomy, large stone found in ter- minal ileum with com- plete obstruction
6	Common duct duodenal fistu- la	50, N, F.	Cholecystitis with cholelith- iasis	Cholecystectomy with drainage of empyema
7	Perforation into small intes- tine with gallstone ileus	59, W, M.	1 Carcinoma of prostate 2 Obstruction high in G I tract, probably stomach 3 Carcinoma of stomach	Exploratory laparotomy; re- moval of gallstone from jejunum with relief of obstruction
8	Cholecystenteric fistula?	69, N, F.	Intestinal obstruction near ileocecal valve	Exploratory laparotomy, removal of gallstone from terminal ileum; gallstone 3 cm. in diameter was producing complete ob- struction

PERFORATIONS (INTERNAL BILIARY FISTULA)

RESULT	STONES	BACTERIOLOGY	PATHOLOGY
Wells			
Well	None seen; no history of ever passing any		Many adhesions about gall bladder, large fistula between gall bladder and duodenum 1 cm. thick and 2 cm. long, gall bladder small and thick-walled, no stones
Well	+ (Not yet extended into G.I. tract)		Many adhesions between gall bladder and cecum and small intestine and colon; fistula between gall bladder and colon through which a stone had eroded, still adherent to the fistula; numerous stones had also eroded gall bladder wall and one had almost perforated into the peritoneal cavity. Final diagnosis: chronic cholecystitis with cholelithiasis with perforation into colon
Died (autopsy)	+	(Stone in ileum missed at operation)	Cholelithiasis and chronic cholecystitis, fistula between gall bladder and ileum, large gallstone obstructing ileum, adenocarcinoma (at other end of gall bladder) of gall bladder with extension of tumor into liver, although partial obstruction of duodenum relieved at operation, gallstone in ileum producing complete obstruction was missed
Well	+		Large gallstone in ileum producing complete intestinal obstruction, fistula not visualized
Died on table under spinal anesthesia (no autopsy)	+		Large gallstone removed from ileum, which was producing complete intestinal obstruction; gall bladder palpated and found to be bound down by adhesions and full of stones, fistula not seen on autopsy
Died on 8th P.O. day with temperature of 103° F (autopsy)	+	(Stone had almost perforated into duodenum)	Common duct very dilated measuring 2.5 cm. circumference, thick-walled and has a bright yellow mucosa, contains a dark brown gallstone 1 cm. in diameter about 7 cm. from its main opening into duodenum. Just above this the mucosa of the duct is elevated and darkened over the stone, in the center of this area is a perforation through which stone can be seen and through which gallstone was about to perforate into duodenum; no peritonitis
Improved (died the next year of carcinoma of prostate)	+		Cholelithiasis, cholecystitis, chronic; perforation of gall bladder with fistula to small intestine, intestinal obstruction due to gallstone 2 cm. in diameter; carcinoma of prostate
Well	+		No fistula was palpated, the surgeon believed there was a dilated common duct through which stone had passed, but did not visualize the gall bladder region

(Table VI continued on following pages)

TABLE

NUM BER	TYPE OF PERFORATION	AGE, RACE, AND SEX	PREOPERATIVE DIAGNOSIS	OPERATION
37	Perforation into 4 coils due to carcinoma of gall bladder (perforation into colon)	69, W, M.	Carcinoma of liver	No operation <i>Autopsy (died)</i>
38	Cholecystocolic fistula	66, Chinese, M	Autopsy record: Extensive str. infection of genital and surrounding structures, septicemia, diabetes	No gall bladder operation GI service
39	Cholecystoduodenal fistula	63, W, M.	Intense jaundice, obstinate constipation, emaciation, Dr. Osler's service 1889, moribund	No operation; medical service
40	Cholecystoduodenal fistula	43, W, M.	Tuberculous meningitis	No operation, medical service
41	Perforation into duodenum due to carcinoma of gall bladder	69, W, M	1 Pulmonary tuberculosis with tuberculous glands pressing on duodenum, causing intestinal obstruction 2 Carcinoma of GI tract with metastases to liver	No operation

1950, Stolck, 1939). There is often a necrotizing enteritis at the site of lodging of the stone and an impaired blood supply to this region. The possible development of these types of bowel damage is of interest in view of the recent demonstration of the protective effect of penicillin in closed isolated jejunal loops in rabbits (Harper and Blain, 1945) and in strangulated low ileal obstruction in dogs (Blain and Kennedy, 1946).

*Report of cases*—All foregoing cases in this series have been grouped according to location with respect to type of perforation of the gall bladder. The age, sex, race, preoperative diagnosis, operation, and result for each patient are indicated in Tables I, III, and IV. In addition the presence or absence of gallstones has been noted and the pathologic diagnosis (autopsy or surgical pathologic report) summarized. Cowley and Harkins (1943) and many others have studied the symptoms and other features of gall bladder perforations. Inasmuch as this study has been concerned primarily with the cases in which gall bladder perforations have been responsible for intestinal obstruction only those patients who developed intestinal obstruction will be discussed in any detail.

#### CASE REPORTS

*Intestinal Obstructions Associated With Type I (Niemeyer) Perforations of the Gall Bladder*—Five (45 per cent) of the cases in this study in which in-

POST B

RESULT	STONES	ETIOLOGY	PATHOLOGY
(Patient Not Operated Upon)			
Died (autopsy)			Carcinoma of gall bladder with extensive involvement of liver, metastases to lungs, spleen, and kidneys. Cholecystocolonic fistula; peritonitis and lesions ascites, bilateral hemothorax; fistula due to carcinoma of gall bladder.
Died (autopsy)	+		Cholelithiasis with obstruction of cystic duct and cholecystocolonic fistula; chronic cholecystitis, early biliary cirrhosis of liver, extensive necrosis of peritoneum.
Died (autopsy)	+ (None in intestinal tract)	(First autopsy performed at J H H)	Common duct very dilated and connected to lumen of duodenum by a fistula (round of course, measuring 1 cm in diameter), common duct full of stones; normal opening of common duct in duodenum not dilated. Gall bladder contracted about 1/2 size, stones in common duct, no stones in intestine, no microscopic report.
Died (autopsy)	None found		Incidental finding at autopsy was fistula between gall bladder and duodenum, gall bladder very shrunken, cystic and common ducts bile-stained and not dilated, ampulla of Vater patent no stones, tuberculous meningitis.
Died (autopsy)	+	Gall bladder, gamma str and B coat	Adeno- and colloid carcinomas of gall bladder, metastases to liver, regional lymph nodes, omentum. Cholelithiasis, fistula between gall bladder and duodenum, multiple abscesses in liver and liver. Stone in common duct near ampulla, dilated bile ducts, pancreas, biliary cirrhosis; pulmonary tuberculosis.

intestinal obstruction was an important factor may be classed as "volvulus free perforations." Two of these resulted in multiple abdominal abscess formation rather than an out-and-out generalized peritonitis. In neither case was the etiology of the abscess formation diagnosed and both patients died. Biliary peritonitis (Harkins, Harmon, and Hudson, 1936) may exist concurrently with intestinal obstruction in these cases and the two conditions may jointly increase the seriousness of each other and to render the results demoralizing. Of the group of five patients who developed intestinal obstruction, the first three

TABLE VII. NINERIK TYPE II (CHRONIC SUPRACALCULUS BILIARY FISTULA) OPERATIONS.  
F. W. H. 1937

Surgical patients recovered	5
Surgical patients died	3
Total surgical cases (38 per cent mortality)	8
Autopsy cases (patients not operated upon)	5
Total cases	13
Cases with intestinal obstruction* (5 cases of gallstone ileus) (0 cases of inflammatory or paralytic ileus)	5

\*Thirty-eight per cent with intestinal obstruction



were operated upon with two deaths (67 per cent mortality) and the other two obstructions were discovered at autopsy in patients who had had no operation.

CASE 4.—A 46 year old white man had had difficulty since boyhood with epigastric fullness and nausea after eating. He was admitted to the gastro-intestinal clinic because of right upper quadrant pain. A gall bladder was done but was unsatisfactory. While it was being repeated he was suddenly seized with a severe pain in the abdomen, not too well localized but apparently more intense in the region above the umbilicus. He was cold and clammy when brought to the accident room. The pulse was rapid and he was in severe agony. Temperature was 101.6° F., pulse, 112. The blood pressure was 140/85 and the respirations were 24. He was obese and not jaundiced. There was marked spasm and a rebound tenderness in the right upper quadrant. There was exquisite tenderness on pressure in this region. The boyhood symptoms had been more severe for the past five years, especially after ingestion of fried or fatty foods. At such times there was eructation, a feeling of epigastric fullness, a bad taste in the mouth, and heartburn. In the past five days the symptoms had been more severe than ever before and were associated with vomiting and constipation. The preoperative diagnosis was that he had an acute exacerbation of a chronic cholecystitis with cholelithiasis, and that there was an associated paralytic ileus. Because the patient was very obese and the gall bladder inaccessible and very friable at operation drainage of the gall bladder region was all that was carried out. A large hole was seen in the gall bladder fundus. This was now partially plugged with omentum. There were several large gallstones free in the peritoneal cavity which also contained a fair amount of bile stained fluid. This peritoneal fluid was cultured on blood agar and on broth without any growth. The patient was improved as a result of the operation but returned one year later with a history of symptoms referable to the gall bladder of fifteen weeks duration. He was given admission slips but refused further operation and has not been heard from since.

CASE 5.—A 64 year-old white man entered the hospital with symptoms of an acute abdominal condition the onset of which had occurred ten days prior to admission. There had been partial intestinal obstruction and pain which was localized chiefly to the epigastrium. At the exploratory laparotomy done soon after admission a large abscess was found in the anterior part of the right lumbar region and the abdominal cavity contained a large amount of blood. The appendix was not found at operation and the cause of the abscess remained unknown. Inasmuch as this operation was performed before the advent of the Wangenstein and Miller-Abbott tubes, a loop of bowel was brought into the abdominal incision. During the next twenty-four hours there was no bowel movement. An enterostomy was done on the exposed loop, but the patient died two weeks after operation. Postoperatively the temperature had always been subnormal and there had been a leukocytosis ranging around 24,000. Culture of the abscess at operation showed *Bacillus coli*.

At autopsy was revealed a gangrenous gall bladder which had perforated in two places. These perforations communicated with a large abscess in the right lumbar region. There were many other abscesses in the region of the cecum and in the pelvis. The intestines were greatly knotted and bound together producing the obstruction. There were no gallstones. The final diagnosis was gangrene of cholecystitis; rupture of the gall bladder with formation of a large abscess in the right lumbar region and many small abscesses in the mesoceleal region and pelvis; chronic widespread adhesive peritonitis; operation wound (drainage of abscess and enterostomy); and acute enteric encephalitis.

CASE 8.—A 47 year old white man entered the hospital with a chief complaint of abdominal pain of ten days' duration. The history, which was judged to be rather unreliable, was as follows. There had been anorexia for two years but digestion had been normal. There had been very vague right upper quadrant pains several years before. There was no eructation, nausea, or vomiting. Seven months before admission the patient had experienced pain in the epigastrium which lasted three or four days. This pain was unrelated to eating and was not associated with nausea or vomiting. Bowel habits had been regular until the onset of the present illness. There had been no clay colored or tarry stools and there was no jaun-

die Ten days prior to admission he had a pain in the epigastrium. This pain was at first dull and intermittent but after the ingestion of a laxative became severe and colicky in character. There were many bowel movements but no nausea or vomiting. The pain persisted in the epigastrium until three days prior to admission, when it became localized in the right lower quadrant. There was associated generalized abdominal tenderness and soreness. At this time the attacks of colic became so severe that he doubled up in pain and there was nausea and vomiting. The vomitus was green and bitter. He was admitted to another hospital and then transferred to this hospital. On admission the temperature was 100° F., pulse was 90, respirations were 36, blood pressure was 135/70, and white blood cell count was 15,000. He appeared acutely and chronically ill. The abdomen was distended and there was generalized tenderness and muscle spasm which was most marked in the right lower quadrant. There was also a palpable, exquisitely tender mass in the right lower quadrant. The abdomen although tympanitic to percussion was dull in this area. The abdomen was silent to auscultation with occasional series of metallic tinklings. A Miller Abbott tube was introduced and intravenous fluid therapy was begun. The following day the distention and pain were more marked. On the basis of the clinical and x-ray findings a diagnosis of acute complete intestinal obstruction due to an inflammatory or neoplastic cecal mass was made. On the third hospital day an exploratory laparotomy was performed. A mass which was judged to be of neoplastic origin was found in the region of the cecum. A terminal ileostomy was done. The patient died on the second postoperative day with a fever of 102° F. An autopsy revealed a chronic cholecystitis and cholelithiasis. There was an ulcer in the mucosa of the gall bladder which had burrowed through the wall dissecting the layers. This had finally perforated and through the perforation hole had leaked down the paracolic gutter to produce an inflammatory mass. The mass was the cause of a complete intestinal obstruction. A smear made from the peritoneum in the region of the mass showed no organisms but a culture grew *Bacillus proteus*, *Escherichia coli*, and an alpha *Streptococcus fecalis*.

It is significant that at the clinical pathologic conference at which this case was presented the correct diagnosis was no more suspected by the participants than it had been while the patient was alive.

The other three cases in which free (Necrotic type I) perforations resulted in intestinal obstructions were essentially cases of generalized peritonitis with resultant paralytic ileus. In two of these the correct diagnosis was made preoperatively although in one it is not clear that generalized peritonitis was suspected. The third patient was treated so long ago that only the autopsy record is available.

CASE 11.—This case is from the early autopsy records and is one in which a thickened and inflamed gall bladder was found to be full of purulent exudate. It was perforated posteriorly forming a large abscess cavity. There was a stone in the gall bladder and there were two stones in the abscess cavity. There was a generalized peritonitis associated with paralytic ileus. The viscera such as the stomach and liver were covered with fibrinous adhesions. It is of interest that cultures of the abscess cavity, the surfaces of the spleen and liver, and the peritoneal fluid all yielded pure growths of the *Bacillus of Flexner*.

CASE 12.—A 59-year-old woman who was tall, thin, and unmourished was brought to the hospital by the police. They had found her lying alone in a gutter. The history was hard to obtain and was not reliable. She had supposedly lived for years on doughnuts and sausage. She had been constipated for a long time. She had been growing progressively weaker for two years with intermittent painless, and on admission could not stand upright. For the past few days prior to admission she had had incontinence of urine. She had had increased markedly during the three days before admission and at the time of admission she complained of abdominal pain and drowsiness. On admission the white blood cell count was 44,000 (94.5 per cent polymorphonuclear leucocytes), temperature 97.4° F., pulse 100, respirations were 20, and the blood pressure was 140/62. Physical exam-

ination revealed a filthy, drowsy, uncooperative, jaundiced, malnourished, weak old man in no apparent pain. There was moderate abdominal distention and there was some tenderness on pressure over the whole upper abdomen. This was perhaps more marked in the epigastrium and under the right costal margin. There was no much spasm and no masses were palpated. The clinical impression was given as "dehydration, probably with acidosis; senility and arteriosclerosis; icterus (with many scratch marks) due probably to gall-stones." The leucocytosis suggested probable empyema of the gall bladder following cholecystitis. She refused an operation and died six weeks later of heart failure. During the first three weeks in the hospital temperature ranged around 102 to 103° F. In the fourth week she had severe abdominal pain, marked distention, right upper quadrantal pain, spasm, and tenderness. At this time the temperature ranged between 103 and 104° F and the jaundice began to increase. Atrial fibrillation developed and she died with pulmonary edema. The last few days the abdominal distention was greater and there were no audible peristalses. The abdomen was rigid and there was obstipation and vomiting. The final clinical impression was acute and chronic cholecystitis and cholelithiasis with necrosis of the gall bladder probably causing generalized peritonitis and paralytic ileus. The findings at autopsy were as follows: Cholelithiasis with impaction of one stone in common duct near papilla; obstruction and dilatation of common duct; jaundice; ulcerative cholecystitis with perforation of the gall bladder wall; and local and generalized fibrinopurulent peritonitis. There was also bilateral hydrothorax, pulmonary edema, and other findings referable to the heart disease.

**Intestinal Obstructions Associated With Type II (Niemeyer) Perforations of the Gall Bladder**—Only one of the eleven cases of intestinal obstruction reported was associated with a perforation of the gall bladder with localized abscess formation. The patient was operated upon and recovery resulted. This was a complicated case in which intestinal obstruction followed an operation for a ruptured appendix. The coexistent distention obscured for a time the fact that the acute empyema of the gall bladder had led to its perforation and the development of a large pericholecystic abscess which was walled off by the stomach, colon and liver. It is not known whether the appendicitis was the cause of the result of the cholecystitis. It is also not definitely known whether the obstructive symptoms were the result primarily of the pericholecystic abscess, a paralytic ileus, or both.

**CASE 24**—A 41 year old colored man entered the hospital complaining of abdominal pain of one week's duration. This pain was associated with nausea and vomiting but there had been no normal bowel movement every day of the illness. Although it was most marked in the right lower quadrant it was generalized. On admission the white blood cell count was 15,000, the temperature 99.4° F, pulse 96, respirations were 24, and the blood pressure was 120/80. The abdomen was distended and was diffusely rigid and tender. The diagnosis was acute dysentery with peritonitis and peritonitis. An appendectomy with drainage was performed. Microscopic examination of the appendix showed acute and chronic appendicitis with a large amount of fibrinous exudate on its serosal surface. Postoperatively the patient had no relief, the abdominal distention increased in spite of Wangenstein suction, and the pain was more severe. By the fifth postoperative day the patient was very ill. The temperature was 102° F and the white blood cell count was 25,000. On this day a hard mass was palpated under the right costal margin. This area was about 4 by 4 cm. in diameter and was exquisitely tender. A diagnosis of acute cholecystitis was made and a cholecystectomy was performed. At operation the gall bladder was found to be perforated by the appendix and liver. Although it had perforated, the gall bladder was not free in the peritoneal cavity. About 40 cc. of thick dark bile was aspirated from its lumen. Its surface was glazed and not white like normal. The aspirated bile had a fecal

odor. Microscopic study of the gall bladder revealed that only a small portion of the mucosa remained. There was a heavy infiltration of the wall by both polymorphonuclear leucocytes and round cells. Areas of gangrene extended all the way through the wall. Cultures of the gall bladder contents produced a heavy growth of bacteria. The postoperative course following this operation was uneventful and the patient was cured.

**Intestinal Obstructions Associated With Type III (Niemeier) Perforation of the Gall Bladder.**—Five cases (45 per cent of the total of eleven cases) of intestinal obstruction associated with all types of gall bladder perforation were seen in connection with biliary-intestinal fistulas. All of these were directly due to gallstone ileus. All of the patients were cured. All of the five died (a mortality of 40 per cent).

**CASE 11**—A 63 year old white woman came to the medical dispensary complaining of abdominal pain and of having vomited fifteen times during the last 24 hours. The vomiting was at first green and later was brown and foul smelling. Her family physician had been called five or six years before that she had gall bladder trouble. She said that she had lost about 25 pounds of weight in the past several months. During this time she had had severe colicky, cramp-like abdominal pains occurring in the mornings and not related to meals. She had become increasingly constipated without any essential changes in the character of the stools. The stools were not bloody or tarry in character. There had been no jaundice. There was a nodular mass in the right upper quadrant which descended to the level of the umbilicus. The clinical impression was that she had either carcinoma of the gall bladder with pressure on the duodenum causing high intestinal obstruction or hydrops of the gall bladder associated with carcinoma of the stomach which had metastasized to the liver. At operation the gall bladder was found to be acutely inflamed and full of stones. At the fundus was a carcinoma which had extended into the liver. At the other end of the gall bladder near the cystic duct the gall bladder had perforated into the ileum. Six black faceted stones and a large gallstone were evacuated from the organ, a drain was put into it, and the abdomen was closed. The gall bladder grew back. The patient died on the first postoperative day and at autopsy a large gallstone was found in the ileum producing complete intestinal obstruction. Although the surgeon found partial duodenal obstruction at operation the complete intestinal obstruction due to the presence of a large gallstone was missed. The diagnosis was as follows: cholelithiasis and chronic cholecystitis, fistula between the gall bladder and ileum, large gallstone obstructing the ileum, and adenocarcinoma of the gall bladder with extension of the tumor into the liver.

**CASE 12**—A 49 year old woman was admitted on April 11, 1935, complaining of vomiting and right upper quadrant pain of six days' duration. She had had attacks of vomiting and right upper quadrant pain for twenty five years or more. There had been an intolerance for fatty and fried foods for many years. There had never been any jaundice. She had been told by a physician that these "bilious attacks" were due to gall bladder disease and was put her on a low fat diet. She remained well while on this diet but as soon as she got from it the symptoms would return. In the past the attacks had been recurrent every two or three days. They disappeared as suddenly as they began. Six days prior to admission she drank several highballs and ate some pie and cake. She was awakened from sleep with a severe right upper quadrant pain and was unable to get up and felt a dull ache in this region. Sooner than she had expected the pain to subside, it was gone. On admission she was acutely ill and dehydrated. Temperature 101.5, pulse 92, respirations were 32, and blood pressure was 120/80. The abdomen was full but soft in the right upper quadrant. There were generalized tenderness without point pain. There were no hiccups. A roentgenogram of the abdomen showed dilated loops of small intestine in the right upper quadrant, indicating the presence of obstruction. A diagnosis of intestinal obstruction was made by the surgical staff. A medical consultant made a diagnosis of high ileal obstruction.

possible gall bladder disease. An exploratory operation was done and the small intestine was found to be considerably dilated while the large bowel was collapsed. Palpation of the terminal ileum revealed a mass 10 cm proximal to the ileocecal valve. This mass was believed to be a gall-stone. It was removed from the ileum and found to be a fairly large gall-stone. Palpation of the gall bladder revealed at least one other large stone still contained within it. Because of the condition of the patient it was decided to defer cholecystectomy until a later operation and to watch her carefully in the meantime for a recurrence of gallstone obstruction. On July 6, 1945, after an uneventful recovery and interval, a cholecystectomy and closure of a cholecystogastric fistula were carried out. There was a 5 Gm stone in the gall bladder and there was a good deal of chronic inflammation in the gall bladder wall. Recovery from the second operation was also successful.

[illegible]

CASE 13. A 50 year old white man was admitted to the hospital with a history of nausea, weakness, and weight loss of ten weeks' duration. The patient had been ill for twelve days prior to admission. He was seized with a severe, cramping abdominal pain associated with vomiting. He vomited six times and after the last episode. The patient described the vomiting as green at first and later brown. He was unable to eat or take any food or liquid for several days. There was no bowel movement for several days. There were several times and had transient crampy pains at the lower abdomen. The patient was pale and there were no concomitant with the vomiting spells. On the day of admission there was fecal vomiting. The temperature was 98.6° F, pulse 80, respirations were 20, and the blood pressure was 120/80. He complained that he had been unable to keep any food in the stomach for the past three days and he had no energy. The hemoglobin was 12 per cent. He was obviously ill, a white man who appeared to be about 50 years old. He was thin and had pain in the epigastric region although there was no definite tenderness or rigidity in the epigastrium. There was a slight rigidity in the right upper quadrant. The abdomen was not markedly distended. The liver and spleen were not palpable. On rectal examination



testine by way of the dilated common duct, such a large stone must have caused erosion of either the ampulla of Vater, common duct wall, or gall bladder wall. Furthermore, if the two cases referred to in this paragraph are excluded they actually strengthen our main argument and we include them for completeness. Without them six out of nine intestinal obstructions due to gall bladder perforations (67 per cent) were caused by inflammatory mechanisms rather than by gallstone ileus. If the two cases are included, six out of eleven intestinal obstructions due to gall bladder (and bile duct perforations [55 per cent]) were caused by inflammatory mechanisms rather than by gallstone ileus. In either instance the inflammatory obstructions represent a majority.

### DISCUSSION

Among all the causes of intestinal obstruction, perforations of the gall bladder are not common. On the other hand, in this series, intestinal obstruction occurred in nine of thirty-nine demonstrated perforations (23 per cent) and, in eleven of a total of forty-one probable and demonstrated perforations (27 per cent). Because this condition is not often considered in the differential diagnosis of intestinal obstruction, it is frequently unrecognized when it does occur. Failure to make a correct diagnosis carries with it a high mortality, whereas the mortality rate may be low if the true pathologic state is suspected preoperatively.

In spite of the great reduction in the mortality from intestinal obstruction in general which has resulted from advances in fluid and electrolyte replacement (Hewell and Hognet, 1912; MacCallum, 1920; Haden and Orr, 1923; Collier, 1940, and others) and from the development of intestinal suction and intubation (Wangersteen, 1942; Miller and Abbott, 1934, and Johnston, 1939) there is still a considerable annual loss of life due to this condition. It is important, therefore, to be aware of all the unusual types of obstruction which are commonly overlooked. The valuable effect of all the rare and unusual types of intestinal obstruction which have not commonly been considered and therefore frequently diagnosed early and of which the present condition is a significant example, is obvious as important in maintaining the present level of intestinal obstruction as are the factors of infection and strangulation.

Other writers (Waters, 1926; Bartlett and Bartlett, 1926; Greene and Coe, 1940 and Hanna and Eger, 1943) have mentioned intestinal obstruction in the differential diagnosis of their reported cases of perforation of the gall bladder. Occasional cases of actual mechanical intestinal obstruction associated with gall bladder perforations (exclusive of gallstone ileus) are to be found in the literature. For example, Edwards, Gerwig, and Guyton (1941) in reporting twenty-one cases of acute cholecystitis with perforation into the peritoneal cavity studied at the Church Home and Infirmary and at the University Hospital, Baltimore, described a case of a 59-year-old man who had suffered severe right upper quadrant pain for several years. He had noted continuous pain for more than twenty-four hours before being seen. On admission he was critically ill with vomiting and distention; skin was dry and jaundiced and the abdominal muscles were fairly rigid throughout. Tenderness was exquisite and diffuse and there

was a mass in the right upper quadrant. On exploration, the hepatic flexure of the colon was found to be densely adherent to the gall bladder and was obstructed. A perforation of the gall bladder had occurred just lateral to its fixation to the colon. Gallstones and bile were found in the free peritoneal cavity. When the gall bladder was dissected from the colon the obstruction was relieved.

In the present series of cases intestinal obstruction associated with perforation of the gall bladder was not due to gallstone ileus in six of nine established cases and in six of a total of eleven probable and established cases; but resulted from the inflammatory reaction or adhesions following perforation of the gall bladder. Perforation of the gall bladder should, therefore, be considered in the search for the cause of intestinal obstruction of obscure origin.

#### SUMMARY

A study of forty-one acute, subacute, and chronic gall bladder perforations of which thirty-nine were confirmed at operation or autopsy, seen at this hospital on the surgical service over the last twenty years (twenty-nine cases), and at the autopsy table since 1899 (twelve cases), eleven cases (27 per cent of the total) were found to be associated with intestinal obstruction. Only five of these eleven cases (45 per cent) were instances of the classical gallstone ileus, three of which were confirmed by actual visualization of the fistula. The other six (55 per cent) were not due to the formation of cholecystenteric fistulas but rather to other mechanisms produced by acute or subacute gall bladder rupture. The relative rarity of these lesions and the obscurity of the symptoms produced by them led to a low percentage of correct diagnoses and to a high percentage of fatalities.

#### CONCLUSIONS

Intestinal obstruction of obscure origin may sometimes be due to perforations of the gall bladder. In this series about one-fourth of such perforations resulted in intestinal obstruction. In puzzling cases, gall bladder disease should be considered in order that intestinal obstruction produced by gall bladder perforation might be recognized.

In this series, intestinal obstruction due to gall bladder perforation was more often (55 per cent of all cases, 67 per cent of confirmed cases) due to acute or subacute perforations with resultant inflammatory paralytic or mechanical obstruction, than (45 per cent of all cases, 33 per cent of confirmed cases) to chronic perforations with resultant classical gallstone ileus.

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### Urology Award

The American Urological Association offers an annual award "not to exceed \$500" for an essay (or essays) on the result of some clinical or laboratory research in urology. Competition shall be limited to urologists who have been in such specific practice for not more than five years and to residents in urology in recognized hospitals.

For full particulars write the secretary, Dr. Thomas D. Moore, 569 Madison Avenue, Memphis, Tenn. Essays must be in his hands before May 1, 1947.

The selected essay (or essays) will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Hotel Statler, Buffalo, N. Y., June 30 to July 3, 1947.

## Review of Recent Meetings

### TWENTY-SIXTH MEETING OF THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

DETROIT, MICH., May 29-31, 1946

F. C. FISHBACK, M.D., WASHINGTON, D. C.

**The Management of Thoraco Abdominal War Injuries,** Reeve H. Betts, Boston.—The mortality rate of thoracoabdominal injuries was reduced from the 50 to 60 per cent of World War I to a level comparable to straight abdominal injuries by the utilization of adequate anesthesia, the transthoracic approach, the preoperative restoration of disturbed cardio-respiratory physiology, adequate blood replacement, before, during, and after operation, and the maintenance of a clear airway at all times. In these wounds, the diaphragm is always injured. A defect in the diaphragm will produce a sucking wound. The diagnosis may be obvious or very difficult. Thoracic wounds may produce abdominal pain and muscle spasm. Absent peristalsis may indicate bowel injury, but is not reliable. A wound as high as the fourth rib anteriorly may penetrate the abdomen. Ninety per cent of chest wounds may invade the belly, ten per cent of abdominal wounds may penetrate the chest. In penetrating chest wounds, an intact diaphragm eliminates intraabdominal injury. Thoracotomy permits the prompt restoration of normal intrathoracic physiology, which lessens shock. Large intrathoracic injuries are best controlled when given, they should be run in slowly. The approach to the chest wounds should be individualized. The transthoracic approach affords better exposure for lesions of the esophagus, stomach, splenic flexure of the colon, and dome of the liver. Repair of the diaphragm is easier from above; the pleura is more easily washed out, and there are fewer postoperative pulmonary complications. Chiotomy is necessary for repair of injuries to the lower, later portions of the esophagus and sigmoid. Separate incisions may be used, or the thoracotomy incision may be extended downward across the costal margin. More rapid reexpansion of the lung is attained without underwater drainage, but frequent pleural aspirations may be necessary. A clear airway is maintained at all times by catheter aspiration or bronchoscopy drainage. The mortality in these cases parallels the severity of the wounds. The mortality from right-sided wounds is lower than from left-sided wounds. Pulmonary complications accounted for more deaths than did abdominal complications. Prompt reexpansion of the lung and a clear airway reduced pulmonary complications. Deaths on the first postoperative day were often associated with a uremic syndrome, the result of prolonged shock and concomitant renal anoxia. The mortality in the forty-eight cases reported by Dr. Betts was 21.0 per cent.

In the discussion, Col James H. Forsee mentioned the lack of statistics for these combined wounds in World War I, but pointed out that abdominal wounds alone carried a 60 per cent mortality in 1916. In World War II, 1,500 exclusively thoracic wounds carried a mortality of only 7 per cent. Dr. Evans Graham suggested that the complication of uremia might be the result of the use of incompatible blood in transfusion. Dr. George Finney said that in the Okinawa campaign, 40,007 units of blood (O type) were used without cross matching, and with but two immediate reactions. Dr. Frank Berry stated that in the event of urgent need for a transfusion, an O type blood of low titer was best; he emphasized that all blood should be refrigerated. Dr. Emilie Holman said that these posttransfusion deaths with anuria were the result of hemolysis, hemoglobinuria, and the production of hemo-

Several papers including the Presidential Address, have appeared in the October, 1946, issue of the *Journal of Thoracic Surgery*.

Received for publication, Nov. 6, 1946.



**The Treatment of Organizing Hemothorax by Pulmonary Decortication.** W. M. Tuttle, Detroit.—Decortication is an old operative procedure, which was discarded after a relatively short trial because of poor results. The conventional treatment of hemothorax had been repeated aspirations, but there was a residual of five to ten per cent in which empyema or crippling fibrothorax occurred. In 1912, Smithy had noted the high incidence of invalidism in these cases; the x ray showed a fluid level but aspiration yielded no fluid and the patient had a contracted chest. The first decortication for organizing hemothorax was done in the African campaign (1913) by Major Thomas H. Barford. Dr. Tuttle reported the results of decortication in 140 cases; there were no deaths in the series. Fifty one presented gross infection, and eighty nine did not. Two-thirds of these patients had combined thoracoabdominal injuries. Seventy five per cent were due to shell fragments. Two instances occurred without wounds, due to contusion. Seventy seven per cent re-expanded within 48 hours after operation, 19.6 per cent re-expanded within five to six days, and only 4.3 per cent failed to re-expand or developed a fistula. Four and three tenths per cent returned to active duty, 4.5 per cent to limited duty, 31.4 per cent were returned to the zone of interior because of their chest conditions, and 16.4 per cent because of extrathoracic conditions. Decortication is easy in the uninfected cases, but difficult in the infected ones. There were only two wound infections in this series. In the fifty one infected patients (empyemata), primary healing occurred in 47.1 per cent, eventual healing in 45.1 per cent, with a small residual group of only 5.8 per cent having a chronic empyema or bronchopleural fistula. The operation should be done within three to four weeks after injury. Prompt decortication assures an easier convalescence and lower risk of empyema. He emphasized the importance of freeing fissures, getting the lung off the mediastinum, and removing the constricting fibrous sheath so that the lung re-expands to fill the chest at the time of the operation. He used two drainage tubes.

**Total Pulmonary Decortication: Its Evolution and the Present Concept of Indications and Operative Technique.** Paul C. Samson, Oakland, Calif.—Delorme used the term "decortication" first in 1896, although it is improbable that he conceived of the process as peeling off an inflammatory membrane from the pleura. In 1907, Fowler performed an operation for chronic empyema which involved freeing of a constricting membrane. Delorme reported in 1909 two cases, one in 1902 and another in 1903, stating in the latter that he removed a membrane from the pleura. There have been many modifications since then. It was usually carried out with open drainage and irrigations. In 1915, Howard Lillenthal described an operation for acute empyema in which he freed the lung from the diaphragm but not the mediastinum, pointing out that the pyogenic membrane can be stripped off the normal pleura. Moynihan described freeing up the lung when removing a foreign body. Decortication has usually been accompanied by much bleeding. In organizing hemothorax, the pleura remains thin, while the fibrous coat which encircles and parallels the pleura becomes progressively thicker and may even become calcified; the presence of air seems to be conducive to an even thicker fibrous coat. Delay in operation makes decortication more difficult, or even impossible. The chest is opened through a posterolateral incision in the sixth interspace, the liquid or semiliquid clot evacuated, and then decortication is begun with a sharp incision to the visceral pleura. The lung herolates through this incision, and further dissection is carried out with the finger or a peanut dissector. The lung is freed from the mediastinum and diaphragm, and the fissures are separated. Tears in the pleura or lung should be repaired. When pulmonary abscess is present, segmental or wedge resection of the lung is carried out. Three rubber tube drains are inserted, one in the eighth interspace in the posterior axillary line, another in the eighth interspace in the midaxillary line, and a third in the second interspace in the midclavicular line. The chest is flushed out with saline, the lung re-expanded, and the chest wall is then closed in layers. Penicillin is instilled through the upper anterior tube, but no irrigations are done. The tubes are connected with a water trap and the patient is encouraged to breathe deeply. The chief indication for decortication is organizing hemothorax after failure of repeated aspirations. The x rays show a hazy chest with signs of fluid. There is poor expansion of the chest and contraction of the interspaces. In this series of approximately 150 patients, 25 per cent were grossly infected, and in every instance the

lung re-expanded and there were no chronic empyema. Infected organizing hemothoraces should be operated on as soon as possible. In post-traumatic empyema, decortication is indicated rather than rib resection. The rationale of the operation is the early restoration of normal pulmonary function. The "peel" which is removed is not part of the pleura, which remains normal.

In the discussion, Dr. J. M. Chamberlain said to excise the parietal peel last and emphasized the benefits of early ambulation, even getting the patient up on the day following operation, with the resulting prompt restoration of function. Dr. Paulson, in commenting on the difficulty of getting off the visceral peel, said that he removed the parietal peel first, then freed the diaphragmatic pleura, after which he found the visceral peel came off easily. He said he had also carried out decortication for tuberculous pleuritis. Dr. Carl Eggers pointed out that organizing hemothorax is the result of battle casualty, in contrast to the chronic empyemas seen after the last world war, which were the chronic residues of acute infections of the pleura. He recalled how the ribs were embedded in the grossly thickened parietal pleura so firmly that it was impossible to insert a rib spreader, while the visceral pleura layer was relatively thin. Referring to chronic empyema, he felt that an effort should be made to mobilize the lung, especially at the angle of reflection from the chest wall. Dr. E. F. Butler concurred with Dr. Eggers and said that decortication was exceedingly difficult in the old, long established case. Early decortication, preferably within thirty days, facilitates the dissection and minimizes the danger of a crippling fibrothorax. Dr. Fraser Gurd stated that he had used decortication in cases of chronic empyema for many years. He added that he had used chemical decortication with sodium hypochlorite to remove the fibrin mass, many times. Dr. E. D. Churchill recalled that in the army manual on thoracic surgery, which he assisted in compiling, no mention was made of decortication. In the past, a generalized empyema was permitted to localize and then drained. He believes that early decortication represents a new and valuable principle in surgery of the chest; namely, the conversion of a localized empyema into a generalized empyema, with theoretic continuation of the whole pleura, but effectively producing a complete re-expansion of the lung which obliterates the empyema cavity. Re-expansion is more important than drainage in that it restores function and eliminates the need for drainage by collapsing the empyema pocket. Dr. Everts Graham said that these hemothoraces and empyema were different, that empyema was an abscess of the pleural cavity and that a hemothorax was not. He felt that the latter represented a pleural infection, at tenuated by chemotherapy. Dr. Tuttle said that an infected hemothorax was an empyema because the chest contained foul pus and the patients ran a septic fever. He pointed out that decortication antedated the use of penicillin and restated his position that the important thing was adequate re-expansion of the lung. Dr. Samson said that he did not remove the parietal pleura routinely.

**Thoracic Neoplasms in Navy Personnel, W. L. Watson, New York.**—During the years of 1943, 1944, and 1945, 746 cases of cancer and allied diseases (neoplasms) were admitted to the Tumor Service of the Naval Hospital at Brooklyn, N. Y., of which thirty four were intrathoracic neoplasms. Eight cases of mediastinal Hodgkin's disease and two of malignant thymoma were treated by radiation. From a group of twenty five patients with intrathoracic tumors that were treated surgically, fourteen were discovered fortuitously by x ray. In this latter group were two cases of bronchial adenomata treated by pneumonectomy, one case of a schwannoma treated surgically after failure with x ray; a benign lymphoma treated surgically, a left sided teratoma which was excised, a bronchogenic sarcoma treated by pneumonectomy, a capillary hemangioma (or mesothelioma) treated by pneumonectomy, and another bronchogenic carcinoma treated by lobectomy (patient died within four months). The speaker urged routine periodic x rays of the chest.

**Pulmonary Cysts, Herman J. Moersch, Rochester, Minn.**—He presented forty four cases of surgically proved pulmonary cysts and classified them in three groups. Group 1 (twenty five cases), cysts lined with epithelium and having walls containing cartilage, muscle, glands, and other bronchial elements; Group 2 (eleven cases), cysts similar to those in Group 1, ex-

**The Treatment of Organizing Hemothorax by Pulmonary Decortication.** W. M. Tuttle, Detroit.—Decortication is an old operative procedure, which was discarded after a relatively short trial because of poor results. The conventional treatment of hemothorax had been repeated aspirations, but there was a residual of five to ten per cent in which empyema or crippling fibrothorax occurred. In 1912, Smithy had noted the high incidence of invalidism in these cases; the x ray showed a fluid level but aspiration yielded no fluid and the patient had a contracted chest. The first decortication for organizing hemothorax was done in the African campaign (1913) by Major Thomas H. Burford. Dr. Tuttle reported the results of decortication in 140 cases; there were no deaths in the series. Fifty one presented gross infection, and eighty nine did not. Two-thirds of these patients had combined thoracoabdominal injuries; seventy five per cent were due to shell fragments. Two instances occurred without wounds, due to contusion. Seventy seven per cent re-expanded within 48 hours after operation, 18.6 per cent re-expanded within five to six days, and only 4.3 per cent failed to re-expand or developed a fistula. Four and three tenths per cent returned to active duty, 45 per cent to limited duty, 31.4 per cent were returned to the zone of interior because of their chest conditions, and 16.4 per cent because of extrathoracic conditions. Decortication is easy in the uninfected cases, but difficult in the infected ones. There were only two wound infections in this series. In the fifty one infected patients (empyemas), primary healing occurred in 49.1 per cent, eventual healing in 45.1 per cent, with a small residual group of only 5.9 per cent having a chronic empyema or bronchopleural fistula. The operation should be done within three to four weeks after injury. Prompt decortication assures an easier convalescence and lower risk of empyema. He emphasized the importance of freeing fissures, getting the lung off the mediastinum, and removing the constricting fibrous sheath so that the lung re-expands to fill the chest at the time of the operation. He used two drainage tubes.

**Total Pulmonary Decortication: Its Evolution and the Present Concept of Indications and Operative Technique.** Paul C. Samson, Oakland, Calif.—Delorme used the term "decortication" first in 1906, although it is improbable that he conceived of the process as peeling off an inflammatory membrane from the pleura. In 1907, Fowler performed an operation for chronic empyema which involved freeing of a constricting membrane. Delorme reported in 1909 two cases, one in 1902 and another in 1907, stating in the latter that he removed a membrane from the pleura. There have been many modifications since then. It was usually carried out with open drainage and irrigations. In 1915, Howard Lilienthal described an operation for acute empyema in which he freed the lung from the diaphragm but not the mediastinum, pointing out that the pyogenic membrane can be stripped off the normal pleura. Moynihan described freeing up the lung when removing a foreign body. Decortication has usually been accompanied by much bleeding. In organizing hemothorax, the pleura remains thin, while the fibrous coat which encircles and parallels the pleura becomes progressively thicker and may even become calcified; the presence of air seems to be conducive to an even thicker fibrous coat. Delay in operation makes decortication more difficult, or even impossible. The chest is opened through a posterolateral incision in the sixth interspace, the liquid or semiliquid clot evacuated, and then decortication is begun with a sharp incision to the visceral pleura. The lung herniates through this incision, and further dissection is carried out with the finger or a peanut dissector. The lung is freed from the mediastinum and diaphragm, and the fissures are separated. Tears in the pleura or lung should be repaired. When pulmonary abscess is present, segmental or wedge resection of the lung is carried out. Three rubber tube drains are inserted, one in the eighth interspace in the posterior axillary line, another in the eighth interspace in the midclavicular line, and a third in the second interspace in the midclavicular line. The chest is flushed out with saline, the lung re-expanded, and the chest wall is then closed in layers. Penicillin is instilled through the upper anterior tube, but no irrigations are done. The tubes are connected with a water trap and the patient is encouraged to breathe deeply. The chief indication for decortication is organizing hemothorax after failure of repeated aspirations. The x rays show a hazy chest with signs of fluid. There is poor expansion of the chest and contraction of the interspaces. In this series of approximately 150 patients, 25 per cent were grossly infected, and in every instance the

lung re expanded and there were no chronic empyema. Infected organizing hemothoraces should be operated on as soon as possible. In post traumatic empyema, decortication is indicated rather than rib resection. The rationale of the operation is the early restoration of normal pulmonary function. The "peel" which is removed is not part of the pleura, which remains normal.

In the discussion, Dr. J. M. Chamberlain said to excise the parietal peel last and emphasized the benefits of early ambulation, even getting the patient up on the day following operation, with the resulting prompt restoration of function. Dr. Paulson, in commenting on the difficulty of getting off the visceral peel, said that he removed the parietal peel first, then freed the diaphragmatic pleura, after which he found the visceral peel came off easily. He said he had also carried out decortication for tuberculous pleuritis. Dr. Carl Eggers pointed out that organizing hemothorax is the result of battle casualty, in contrast to the chronic empyemas seen after the last world war, which were the chronic residues of acute infections of the pleura. He recalled how the ribs were embedded in the grossly thickened parietal pleura so firmly that it was impossible to insert a rib spreader, while the visceral pleura layer was relatively thin. Referring to chronic empyema, he felt that an effort should be made to mobilize the lung, especially at the angle of reflection from the chest wall. Dr. E. F. Butler concurred with Dr. Eggers and said that decortication was exceedingly difficult in the old, long established case. Early decortication, preferably within thirty days, facilitates the dissection and minimizes the danger of a crippling fibrothorax. Dr. Fraser Gurd stated that he had used decortication in cases of chronic empyema for many years. He added that he had used chemical decortication with sodium hypochlorite to remove the fibrin mass, many times. Dr. E. D. Churchill recalled that in the army manual on thoracic surgery, which he assisted in compiling, no mention was made of decortication. In the past, a generalized empyema was permitted to localize and then drained. He believes that early decortication represents a new and valuable principle in surgery of the chest; namely, the conversion of a localized empyema into a generalized empyema, with theoretic contamination of the whole pleura, but effectively producing a complete re expansion of the lung which obliterates the empyema cavity. Re expansion is more important than drainage in that it restores function and eliminates the need for drainage by collapsing the empyema pocket. Dr. Everts Graham said that these hemothoraces and empyema were different, that empyema was an abscess of the pleural cavity and that a hemothorax was not. He felt that the latter represented a pleural infection, at tenated by chemotherapy. Dr. Tuttle said that an infected hemothorax was an empyema because the best contained foul pus and the patients ran a septic fever. He pointed out that decortication antedated the use of penicillin and restated his position that the important thing was adequate re expansion of the lung. Dr. Samson said that he did not remove the parietal pleura routinely.

**Thoracic Neoplasms in Navy Personnel, W. L. Watson, New York**—During the years of 1943, 1944, and 1945, 746 cases of cancer and allied diseases (neoplasms) were admitted to the Tumor Service of the Naval Hospital at Brooklyn, N. Y., of which thirty four were intrathoracic neoplasms. Eight cases of mediastinal Hodgkin's disease and two of malignant thymoma were treated by radiation. From a group of twenty five patients with intrathoracic tumors that were treated surgically, fourteen were discovered fortuitously by x ray. In this latter group were two cases of bronchial adenomata treated by pneumonectomy, one case of a schwannoma treated surgically after failure with x ray; a benign lymphoma treated surgically, a left sided teratoma which was excised, a bronchogenic carcinoma treated by pneumonectomy, a capillary hemangioma (or mesothelioma) treated by pneumonectomy, and another bronchogenic carcinoma treated by lobectomy (patient died within four months). The speaker urged routine periodic x rays of the chest.

**Pulmonary Cysts, Herman J. Moersch, Rochester, Minn**—He presented forty four cases of surgically proved pulmonary cysts and classified them in three groups. Group 1 (twenty five cases), cysts lined with epithelium and having walls containing cartilage, muscle, glands, and other bronchial elements; Group 2 (eleven cases), cysts similar to those in Group 1, ex





or seventh rib for the lower lobe, (3) individual ligation technique; (4) careful closure of the bronchial stump with interrupted silk sutures over which was placed a pleural graft, (5) water seal drainage until the lung has re-expanded, (6) penicillin locally within the chest, and also intramuscularly until re-expansion occurs; (7) routine bronchoscopy immediately after the operation, and (8) oxygen for ten to eighteen hours after operation. He suggested the use of phrenic nerve interruption after extensive pulmonary resection where the patient complained of pain or a severe sense of tightness of the chest. Fifteen of the patients developed empyema, eleven with fistula and four without. The other complications consisted of seven cases of jaundice, two of pneumothorax, one of hemothorax, one of atelectasis, and one cerebral vascular accident. He advocated the importance of teamwork in assuring success.

In discussing this paper, Dr. R. H. Overholt said that bronchiectasis was not a lobar but a segmental disease and that 30 per cent of these cases were bilateral. He urged the consideration of the pulmonary segment as a surgical unit, adding that branches of bronchi and pulmonary arteries do not cross intersegmental planes. Dr. Meade, in closing said that the series now consisted of 236 lobectomies. He stressed the fact that the procedure is indication for lobectomy in bronchiectasis was the existence of symptoms, and not merely a suggestive bronchogram. In some patients, symptoms began with an attack of virus pneumonia; in others, symptoms had been present many years.

**Pulmonary Function After Adolescence Following Pneumonectomy in Childhood,** Charles Lester, New York.—Dr. Lester stated that this paper constituted a progress report on the cases which he had reported at the Toronto meeting in 1941, with observations on one additional case. He had also included observations made on cardiac output and right ventricular pressure, using the technique of right heart catheterization (insertion of catheter through median basilic vein to the right auricle). All four patients had had their left lung removed. Two presented their tracheas in the midline, in one there was a shift of the trachea and in one the esophagus had moved over. Small pneumothoraces were noted on the left side in the cases with the trachea still in the midline. The lungs had continued to grow but would not equal the combined volume of the two good lungs. Pulmonary artery pressure increased as the lung volume expanded. Distention of the lung may reduce maximum breathing capacity to 55 per cent. Oxygen saturation of the arterial blood is normal with the patient at rest and the lung undistended; with distention of the remaining lung, oxygen saturation falls to 63 to 80 per cent. Cardiac output and pressure within the right heart remain essentially normal. When distention of the remaining lung occurs, dyspnea ensues, and exhaustion comes on earlier.

Dr. Edgar Davis told of a 43 year old pilot, on whom he had performed pneumonectomy for cancer of the lung, who was able to be carried to a altitude of 10,000 feet in a pressure chamber before noting any changes, the first thing noted at that altitude was an abnormality of hearing. Dr. Andre Courmand, the co-author of the paper, discussed the case, saying that one half of these patients in whom pneumonectomy has been performed show some pulmonary distention, which is, however, a mechanical, not a compensatory phenomenon. With excessive strain and dyspnea, distention does occur, and produces anoxia. Pressures in the pulmonary vascular circuit do not increase, the adjustment being affected either by increased rapidity of blood flow or increased capillary diameters. Arterial oxygen saturation is inadequate under stress because of deficient alveolar ventilation or inefficient gas diffusion.

**The Use of Curare in Anesthesia for Thoracic Surgery,** Phyllis Harroun, San Francisco.—Curare has been used routinely in intrathoracic operations at the University of California Hospital since February, 1945. This paralyzing agent may be delivered to patients intravenously during operations. This report described the course of seventy five patients to whom large doses (200 mg to adults and 40 to 60 mg to children) were given at the time of introduction of the intratracheal tube. Curare in these doses produces apnea and permits control of the respiration by the anesthetist. Nitrous oxide and oxygen were the anesthetic agents, and the high frequency cautery could be utilized throughout the entire operation. The patients showed little change from the normal during operations that averaged five and a

quarter hours. The patients awake soon after the termination of the anesthesia. The speaker emphasized that fears of curare, even in large doses, were groundless. In the discussion, Dr. J. A. Weinberg endorsed this method of anesthesia, emphasizing the advantage of being able to use coagulation throughout an operation but advised that curare be kept at a minimum, and suggested using pentothal as an adjunct. Atelectasis would not occur if the breathing were as regular and vigorous when the patient left the operating room, as when he entered. Dr. Dörner said that most postoperative pulmonary complications would be eliminated if routine bronchoscopic drainage were carried out. Dr. H. B. Stephens, the co author, said that this was the best anesthesia he had encountered, and that in this group of cases, no instance of massive atelectasis had occurred.

**Surgery of the Thymus in Myasthenia Gravis.** O. T. Clagett, Rochester, Minn.—The co-existence of a thymic tumor and myasthenia gravis was first reported in 1901, although it was not until 1936 that a case of myasthenia gravis was cured by removal of a thymic tumor. This success led to the removal of a thymus without a tumor, by Blalock in 1939. The course of myasthenia gravis is unpredictable, being characterized by remissions and exacerbations. Of the 191 cases of myasthenia gravis seen at the Mayo Clinic, thirty-two have been operated on. Fifteen of these have had thymic tumors and seventeen showed only thymic hyperplasia. In the tumor group, eleven were men and four were women; in the hyperplasia group, twelve were women and only five men. There was one death in each group. Although Keynes had stated that those cases with thymic tumor offered a poor prognosis, in this series of cases the results were better in those patients with tumor than in those with hyperplasia. The impression is gained that those patients who have been operated on do better than those not operated on. The benefit of surgery may not appear until some time after operation. The optimum dose of neostigmine should be determined and used since this will help the patient to eat and reduce the possibility of aspiration. Preoperatively, the patient should be hospitalized to permit rest and a prophylactic course of penicillin. Sedation should be kept at a minimum. For twenty-four to forty-eight hours after operation, the patient should either be given oxygen or placed in a respirator. Endotracheal anesthesia, augmented at times by local anesthesia is essential. The operation appears to produce little shock. Either a vertical sternalsplitting incision or a posterolateral incision may be used. The thymus is a pinkish yellow, bilobular gland, overlying the pericardium and extending upward toward the neck, anterior to the innominate vessels. The critical period is that immediately after operation. If the patient appears anxious, he should be placed in a respirator. An aspirating set should be kept at hand if there is difficulty in raising secretions. The patient may be tube fed. Early ambulation, i.e., by the third or fourth postoperative day, is customary. Pathologically, some of the thymic tumors proved to be lymphosarcoma, and some carcinoma; some were encapsulated and some were invasive; only contiguous lymph nodes were involved, and there was no spread outside the thoracic cage. These tumors do not respond to x-ray therapy. The thymic hyperplasia of myasthenia gravis might be contrasted with the hyperplastic thyroid of hyperthyroidism.

Dr. Blalock said, in the discussion, that since 1941, he had done total thymectomies; prior to that time, only partial thymectomy had been done. He told of two of his patients who had eventually died, where at necropsy small pieces of thymus were found which had been overlooked at the time of operation. The fact that some patients still die after total thymectomy sustains his belief that the thymus is not alone to blame. He said, however, that the operation offers the best treatment for myasthenia gravis of short duration. When the course of the disease has been prolonged, the results are not so good and suggest that some irreversible change has occurred. Dr. W. E. Adams reported seven patients operated on, without tumor, where the degree of improvement was greater in the estimation of the patient than the surgeon. Operation sometimes reduced the need for prostigmine. He felt, however, that the thymus was but one link in the chain of etiology. His observation that myasthenia gravis did not occur after the menopause, and that with pregnancy, patients improved, made him consider whether some toxic substance existed in the masses. Dr. Oschner spoke of the relationship of the thyroid and thymus and pointed out that hyperthyroidism may offset the effects

of hyperactivity of the thymus. Dr. R. Sweet stated that thymic tumors occur without myasthenia gravis. Dr. W. A. Hudson reported a four year cure after thymectomy where the disease had occurred one year after the menopause. Dr. Clagett said that few people have thymic tumor without having myasthenia gravis.

**Surgical Lesions of the Esophagus Seen in an Army Thoracic Center, Earle B. Kay, Memphis**—During the past three years, over 130 patients with diseases and injuries of the esophagus were seen at this center. Forty operations were performed with one death (2.5 per cent). There were twenty-seven strictures, fourteen of which were due to the ingestion of caustics, and eleven of these were caused by sabotaged alcoholic beverages consumed accidentally while overseas. Twenty-one of these strictures were effectively dilated. Of the six with undilatable esophageal strictures, two had antethoracic esophagoplasties, and four had intrathoracic esophagoplasties. Of the latter, two were total and the other two were at the level of the thoracic arch. There were eight benign intramural esophageal cysts and tumors, of which seven were excised locally, while the eighth required resection and esophagogastric anastomosis. Out of five malignant tumors, three were inoperable and two were treated by resection and esophagogastric anastomosis. There were ten patients with traumatic injuries to the esophagus and eight others had large shell fragments adjacent to the esophagus, two of which had caused localized perforations or diverticuli. Eleven cases of cardiospasm, refractory to the usual dilations were cured by cardioplasty. A marked decrease in the caliber of the esophagus was noted after operation. Twenty instances of congenital short esophagus were encountered; epigastric and nocturnal pain was frequently observed in this group. In the discussion, Dr. R. Sweet advocated the exclusive use of the thoracic incision for all surgery on the esophagus, and urged that the antethoracic esophagoplasty be abandoned for the intrathoracic type of operation. In the treatment of cardiospasm, he favored a long incision, with transverse closure. Dr. F. R. Harper spoke of the remarkable exposure gained by a thoracic incision through the ninth rib bed when it was carried across the costal margin, and suggested its use for exploration of tumors of the adrenal. Dr. Kay, in closing, urged the use of intrathoracic esophageal reconstruction.

**Technical Problems in Surgical Treatment of Carcinoma of the Esophagus and Upper Stomach, John H. Garlock, New York**—A certain degree of standardization has resulted from the review of ten years' experience with surgery for malignancy of the lower esophagus. Adequate preparation before operation reduces postoperative complications. Such preparation includes the use of penicillin both intramuscularly and by nebulization, a thorough dental clean up, repeated irrigations of the esophagus, and the correction of vitamin, electrolyte, and nutritional deficiencies, particularly hypoproteinemia, as well as dehydration. Endotracheal anesthesia is essential because it permits complete control of the patient's respiration and routine bronchial aspiration. The Torek operation has been supplanted by intrathoracic esophagectomy where continuity is re-established by bringing the fundus of the stomach up in the chest, even as high as the apex, and anastomosing it to the proximal esophageal remnant. The stomach is mobilized by closure of the cardia and ligation of the left gastric artery, the vasa brevia, and probably some of the left gastroepiploic vessels. The upper end of the esophagus derives its blood supply from the inferior thyroid arteries. The esophagus is exposed through a left thoracic incision of the sixth interspace, and division of the posterior ends of the fourth, fifth, seventh, and eighth ribs. The anastomosis is done in two layers using interrupted suture and the inner layer apposes mucous membrane to mucous membrane. The stomach is then telescoped over the suture line and the diaphragm is repaired and sutured about the stomach. The utilization of a thoracoabdominal incision has been followed by fewer postoperative complications. The abdomen is opened first through a left rectus incision, and then carried upward and laterally through the costal margin to the eighth left interspace, cutting the diaphragm. The resulting exposure simplifies satisfactory blood dissection. In closing, the wound is repaired in layers. Jejunostomy is done routinely, for post-operative feeding. The chest is drained. In total gastrectomy, intestinal continuity is re-established by suturing the esophagus to the jejunum, and using the Y anastomosis of Roux. The jejunal segment is brought up through the mesocolon. The Y jejunal anastomosis is

preferable to the ordinary jejunal loop. No gastric stump should be left behind, since it may produce pylorospasm. After operation, the patient is placed in an oxygen tent, penicillin is administered, trapped air within the chest is aspirated, and the patient is fed through the jejunostomy. He is given nothing by mouth until the fourth day, but is usually back on a full diet by the third week. In the discussion, there was unanimous praise for the exposure effected by the thoracoabdominal incision. When contemplating total gastrectomy, the initial abdominal incision solves the question of operability before opening the chest.

**Section of the Vagus Nerves to the Stomach in the Treatment of Peptic Ulcer, Lester R. Dragstedt, Chicago.**—Section of the vagus nerves has been done in eighty-two patients over a period of the last three and a half years. Thirty of these patients had abdominal vagotomies, and the remaining fifty-two were operated on transthoracically. The lower four inches of the esophagus must be completely denervated and the proximal end ends of the vagi should be covered with pleura to prevent regeneration. In this series there has been no evidence of regeneration and at least twelve of these patients were operated on more than three years ago. When the abdominal and subdiaphragmatic approach is employed, the esophagus is mobilized by finger dissection and pulled about eight to ten inches. The rationale of the operation is based on the fact that increased acid or hypertonicity of the vagus efferent fibers should augment gastric motility and the secretion of gastric juice. In ulcer patients, the excessive continuous secretion of gastric juice occurs in the stomach in the absence of the usual stimulus of food. Complete section of the vagus nerves abolishes hypermotility and hypersecretion, the ulcer heals, and pain disappears. Evidence was presented showing that vagal section reduces gastric secretion fifty per cent and the secretion of the free hydrochloric acid component, seventy-five per cent. The fact that the stomach when empty may secrete large amounts of gastric juice, and that interference of the vagus nerves reduces this secretion indicates that the cortex has an important role in the hypersecretion of gastric juice in ulcer patients, which is similar to that in the hypersecretion of the parathyroid glands. The concept of ulcer as a psychosomatic disease, Paine's view that the connection between the corticogastric connection is broken. Vagal section does not anesthetize the stomach since the reintroduction of hydrochloric acid will produce pain. The sense of hunger remains unchanged. The lack of response to the stimulation of a sham meal or insulin hypoglycemia after operation indicates that no interference of the vagal secretory fibers has occurred. Gastric tonus and motility is reduced but not abolished; intestinal motility is not decreased. The stomach is kept decompressed for three to four days after operation to avoid acute gastric dilatation. There may be a transient diarrhea for a few days or three weeks. X-ray and gastroscopy afford objective evidence that gastric motility and intestinal motility are normal after vagal section. It is possible that three and a half years is a short time to permit evaluation of final results and to determine whether a permanent regression can occur after that interval. The transthoracic approach may be used for benign ulcers without pyloric obstruction, and for marginal ulcers. The abdominal approach is suggested for gastric ulcers to exclude malignancy, and for duodenal ulcers with acid hypersecretion, so that gastroenterostomy may be done. In discussing this paper, Dr. D. T. Smith pointed out that vagal section in ulcer patients not only stops pain but also stops hunger. Dr. Frank Berry advised that the patient should be cautioned not to overeat, since a long continuous tonus of the pylorus may persist.

**The Management of Thoracic Surgery in the Hospitals of the Veterans Administration, Brian B. Dineen, Washington, D. C.**—This was a brief description of the new organization for thoracic surgery, pointing out that management has been decentralized and that the veterans hospitals as far as possible will be connected with medical schools and will be used for teaching. There should be a plethora of clinical material. Pay scales have been raised and certification by one of the American boards carries an additional 25 per cent wage increase. Under this plan, which lifts the organization out of Civil Service, there should be freedom from administrative duties and red tape.

**Presidential Address: "The Direct Approach to Cardiovascular Disease, Claude S. Elton, Cleveland.**—Although the incidence of cardiovascular disease exceeds all others, the

funds available for the study and treatment of individuals suffering from this group of ailments are most meager when judged by the ratio of the number of such patients to the amount of money available. The relative and actual poverty in this field stands out in sharp contrast to the funds which have been collected for the investigation and treatment of cancer and infantile paralysis. The internist has used indirect methods of study and investigation in this field. However, direct visualization of the heart and blood vessels is now possible and will yield precise knowledge. The program of this meeting displays examples of the results of the direct approach to cardiovascular disease, and includes such subjects as foreign bodies in the heart, the suture of wounds of the auricles and ventricles, the surgical treatment of patent ductus arteriosus, coarctation of the aorta, and the Tetralogy of Fallot. This direct mode of treatment has been applied in contusions of the heart, which are probably more common than penetrating wounds of the heart, and also to the immediate and late repair of peripheral vascular injuries. It has proved useful in extrinsic lesions of the heart where the heart is hindered by fluid, adhesions or scar tissue, and in compression of the heart. The concept of acute and chronic compression of the heart, and torsion and rotation simplifies diagnosis and treatment. Surgery for portal hypertension is another result of the direct approach, as well as orderly procedures for resuscitation, the prevention of pulmonary emboli, and sympathectomy for hypertension and causalgia. The problem of coronary sclerosis has been attacked. Ligation of a main coronary will produce ventricular fibrillation by destroying the coordinating nerve network, but this can be obviated by the supply of a small additional amount of blood to the myocardium either by a graft or the production of intercoronary channels as a result of abrading the surface of the heart or the use of powdered asbestos in the pericardium. In experimental animals, coronary ligation is fatal in 70 per cent, but where the heart has been abraded only 38 per cent die. With survival of a narrow neck of coronary occlusion, new intercoronary channels develop. It is possible that coronary anastomosis might help. Operations to augment a deficient coronary circulation have been done on 37 patients. Neurotomy about the base of the aorta or the thoracic coronary vessels might improve the cardiac circulation. The further use of the direct approach may well lead to the transplantation of arteries, the temporary exclusion of the heart from the circulation, permitting the closure of septal defects or the removal of vegetations, tumors, or thrombi from valves.

**The Tetralogy of Fallot.** Diagnosis and Indications for Operation, Helen F. Tansig, Baltimore. **and The Surgical Treatment of the Tetralogy of Fallot,** Alfred Blalock, Baltimore.—The tetralogy of Fallot consists of pulmonary stenosis, interventricular septal defects, dextroposition of the aorta so that it receives blood from the right ventricle as well as left ventricle, and right ventricular hypertrophy. The usual clinical picture is one of marked cyanosis, normal sized heart, systolic thrill, and right axis deviation. These patients can be helped if it is possible to increase the flow of blood to the lungs, and thereby increase the arterial oxygen saturation. The operation helps only where there is some intercoronary circulation. In the event of congenital absence of the pulmonary artery, operation is impossible. The heart is enlarged and in size to enable it to assume the additional circulation. Avoidance of the pulmonary artery presents an enlarged pulmonary trunk. The pressure in the pulmonary artery must be lower than the pressure in the systemic arterial circulation, to permit the new shunt to function. Twenty per cent of these little patients have a right subclavian arch, the remaining 80 per cent have a left arch. Therefore operation which is done on the subclavian arch, the aortic arch. With dextroposition of the aorta, it runs a "valuable" especially the anterior position. The aorta and the esophagus lying close to the heart and displaced to the left and forward. The age of 5 to 6 years is preferred, but the operation may be done in younger patients, depending upon the degree of cyanosis, and the elevation of the red blood count. Without operation, the chance of survival to puberty is only 30 per cent. With an arterial oxygen saturation as low as 30 per cent an afflicted child can hardly walk. These children exhibit varying degrees of polycythemia which seems to be compensatory. Cerebral thrombosis frequently complicates the picture when the erythrocyte count reaches eight or nine million (or an hematocrit of 70 to 80). Maintenance of an adequate fluid intake lessens the risk of cerebral thrombosis. Venesection is frequently done at the end of operation

to reduce the load on the pulmonary circuit. Dr. Blalock demonstrated the operation with a splendid motion picture which showed the incision through the third interspace anteriorly, ligation of the azygos veins, and measurement of the pulmonary arterial pressure. The average pressure was between 190 and 200 mm. of water; when the pressure is 300 or over, operation is impossible. The operation is easier on the left side, with a right aortic arch. The shunt has been made utilizing the innominate, the common carotid, and subclavian artery. Those anastomoses in which the subclavian artery was used have had the lowest mortality. The right superior pulmonary artery may be mistaken for the main pulmonary artery. The selected systemic artery is divided and its distal end ligated while the proximal segment is occluded with a bulldog. The pulmonary arterial segment, into which the systemic artery selected is to be anastomosed end to side, is occluded gently but securely between soft blood vessel clamps. The anastomosis is done with an everting suture, intima to intima, using 00000 Deknatel silk. Small leaks in the suture line are stopped by finger pressure or an interrupted suture. The mediastinal pleura is then closed. Should the wrong side be chosen for the incision, one may still find suitable vessels for the anastomosis. One hundred forty four cases have been operated on and 118 anastomoses have been done with eighteen deaths (22 per cent mortality). The patients ranged in age from 2 months to 26 years. The innominate artery was used in thirty six cases with twelve deaths; the subclavian artery in seventy two cases with six deaths. It was strongly urged that no one, no matter how greatly skilled, should try this operation on a human without first carrying out the procedure on at least two dogs.

**The Surgical Treatment of Coarctation of the Aorta, Clarence Crafoord, Stockholm, Sweden.**—Dr. Crafoord spoke as he showed a fine moving picture of this operation, which he first performed in October, 1944. For anesthesia, local is used with the endotracheal administration of cyclopropane, oxygen, and nitrous oxide. The intratracheal gas pressure is kept below 25 mm. of water. The approach is through a long S shaped posterolateral incision, exposing an entire rib. A heavy transfusion suture is used to elevate the scapula. The phrenic and vagus nerves are injected with novocain. Two or three pairs of collateral arteries arising from the aorta proximal to the contracted portion, are divided and ligated. The zone of coarctation is excised between clamps and continuity is restored by suture, using 00 oiled silk, each bite being 2 mm. back from the cut edge. The suture does not penetrate the lumen or evert the edges of the aorta. The blood given during the operation is taken from a heparinized donor (1 mg. heparin per kilo body weight). The wound is closed by running sutures in the pleura, periosteal rib bed, and muscles of the chest wall. In discussing this paper, Dr. Robert E. Gross told of his experimental work to determine the practicability of bringing the cut ends of the aorta together. He anastomoses the aorta with 00000 silk using a continuous mattress suture which everts the cut edges. The posterior portion of the aortic suture line is placed first. He divides the necessary intercostal arteries to effect mobilization of the aorta and divides the ligamentum arteriosus. He reported eight cases with two deaths and five good results, and added that some of the benefits may come rather slowly. He urged that the clamps be removed from the aorta gradually to minimize what may be a sudden strain on the heart. In closing, Dr. Crafoord said that he removed the aortic clamps quickly and had not seen any harmful results.

**Complications of the Surgery of Patent Ductus Arteriosus, John Jones, Los Angeles**—Although there have been no wound infections, the frequency of keloid formation in the scars of the anterior incisions caused its abandonment and the substitution of the posterolateral incision, with the section of the fourth and fifth ribs. The occurrence of an aortobronchial fistula was described, in which the patient had six recurring hemoptyses over a period of twenty one months. On exploration, a knuckle of lung was found adherent to the aorta and when the lung was dissected away from the mediastinum, the knots of umbilical tape were recovered which had eroded into both the lung and aorta. On removal of these knots, the rent in the aorta was closed by suture, with recovery. Routine closure of the mediastinal pleura should eliminate this complication. In the fifty three cases where ligation was done, murmurs persisted in five patients and in five more, murmurs reappeared. The persistence or recurrence of the murmur indicates the re-establishment of the fistula. In the eight patients in which

complete division of the ductus was carried out, there has been no recurrence of the murmur. There were two deaths in this series of sixty-one cases. One occurred in a patient whose condition was complicated by a staphylococcus endocarditis where the fistula recurred, with the formation of an aneurysm. The other case was one of rheumatic heart disease with a rigid ductus, death following a leak in the pulmonary artery.

**Complete Division of the Patent Ductus Arteriosus, Robert E. Gross, Boston.**—In a series of 133 cases of surgically treated patent ductus arteriosus, some form of ligation was employed in forty-three instances. Of the forty survivors, there were thirty-two perfect results, four in which the murmur persisted from failure to ligate tightly enough to obliterate the shunt, and four in which the murmur recurred probably because the ligature cut part way through, with re-establishment of the fistula. These failures led to the development of a technique of complete division of the ductus which has now been carried out in ninety cases. The approach is through an anterior incision below the left breast, with section of the second and third costal cartilages and incision of the third interspace. A tongue of pericardium is dissected up and the posterior wall of the ductus freed first. The ductus is clamped doubly at both extremities and after division, the pulmonary arterial end is closed first. The distal clamp is removed and closure is effected by an over and over suture of fine silk, which is returned as a second suture to its starting point. After a similar closure of the aortic end of the fistula, the mediastinal pleura is closed. There were two deaths in this latter series, one from mediastinitis and one from cardiac dilatation. In a child, the patent ductus is soft and pliable and easy to ligate, and any technique should be effective, while in an adult the ductus is often stiff and inelastic, thereby increasing the chance of failure of ligation. Complete division is definitely better because it is just as safe as ligation and more satisfactory in permanently closing these shunts. The discussion was opened by Dr. Crafoord, who told how it took him two and one-half years to sell this operation to the pediatricians in Stockholm. He reported seventy-one cases of patent ductus which he had treated surgically, about one-half by double ligation with the injection of 50 per cent glucose solution between the ligatures, and the other half, usually those with short ducts, by division. In an early case where complete division was being done, the clamp, including the stump, was torn from the aorta. To control hemorrhage, the aorta was clamped above and below the tear, which was closed by suture. This procedure so facilitated the operation, that he now treats the aortic end of the ductus routinely in this manner. This series includes seven infected cases with positive blood cultures. He uses a posterolateral incision between the fourth and fifth ribs, and interposes a pericardial flap at the site of the division. There were two deaths in this series. Dr. Wangensteen said that he deliberately opened the pericardium and developed the tissue plane, separating fibrous and serous pericardium if these layers were not otherwise readily separated. He divides the ductus routinely, a procedure which he has carried out successfully in thirty-three consecutive patients. Dr. A. S. W. Touroff, who in 1940 first reported the successful ligation of a patent ductus in subacute bacterial endocarditis, reported thirteen cases, with eight regarded as cured (well from four to six and one-half years), two operative deaths, and three unimproved. He said that existence of a murmur was not evidence of recanalization, since it could occur even after division, and that it probably was caused by the dilated pulmonary artery. Recanalization was probably due to failure to pull down tightly enough on the knots. Tight ligatures should not cut through, but knots may become loose in the presence of infection. Dr. Edgar Davis told of a case where the murmur was reduced about 50 per cent after ligation, he reoperated and placed two more ligatures on top of the preceding ones, but the murmur persisted. Fascia or fibrin foam should be interposed between the divided ends of the ductus.

**Decortication for Tuberculous Empyema, Fraser B. Gurd, Montreal.**—As a result of a large experience with cases of chronic empyema, decortication had been found frequently to be successful in producing re-expansion of a lung, even after the lung had been compressed for long periods of time. Since the conventional treatment for tuberculous empyema had proved relatively unsatisfactory and left the patient with a permanent reduction in respiratory function, decortication was tried in three cases. Adequate exposure is obtained in these stiffened



chest walls by thoracotomy, done in stages. It is sometimes difficult to find the proper plane of cleavage for dissection. Not only must the fibrous membrane be removed from the surface of the lung but the dissection must be carried to the hilar region if maximum re expansion is to be obtained.

**Lobectomy and Pneumonectomy in the Treatment of Pulmonary Tuberculosis, Richard H. Sweet, Boston.**—In 1943, Drs. Charchill and Klopstork reported six cases of pulmonary tuberculosis treated by lobectomy with two poor results (one now dead) and four good ones. This present series consists of fifty seven additional cases of extirpation done prior to June, 1945. To simplify the evaluation of the procedure and reduce variables, thoracoplasty has not been done after any of these pulmonary resections. Indications for lobectomy were: (1) unfavorable location of cavity, (2) tuberculoma, (3) rigid cavity, and (4) bronchial stenosis. The indications for pneumonectomy were: (1) "destroyed lung," (2) thoracoplasty failure, (3) bronchial stenosis, and (4) technical reasons. These patients were bronchoscoped routinely before and after operation. Chemotherapy reduced or eliminated supuration. Ethos and oxygen were administered through an intratracheal tube; patients were placed on their side. Silk technique was used throughout, and the bronchial stump was always covered with pleura. It was essential that the hilum be free of disease. Dissection of the periphery of the lung was sometimes very difficult. Frequently diseased areas can be seen or felt, where they were not suspected on the basis of previous x ray examination. The chief complications, namely flare ups and empyema, occurred with approximately the same frequency after lobectomy and pneumonectomy; there were thirteen flare ups in twenty seven lobectomies and ten after pneumonectomy. There were two postoperative deaths in the series of twenty seven lobectomies, of the twenty five survivors, five have since died of tuberculosis, seven are alive with tuberculosis, and thirteen appear to be well. In the eleven so-called "elective" cases, seven are well and the other four are living but are still sick. In the tension cavity group of nine cases, there was one postoperative death, four died later, one is living but still sick, and three are well. The two cases of bronchial stenosis resulted in one death and one survivor who still has tuberculosis. There were thirty six pneumonectomies with seven postoperative deaths; of the twenty nine survivors, seven have since died of tuberculosis, five are still sick, and seventeen are well. Out of eighteen who were operated on for "destroyed lung" three are well; of six who a indication was bronchial stenosis, five are well. In five cases where pneumonectomy was done for technical reasons, four are well, in four cases of thoracoplasty failure, three are well. There were two cases of erroneous diagnosis; both proved to be cancer and they are well. Frequently widespread dissemination of tuberculosis in both lungs was noted in the absence of x ray evidence. There is no way to evaluate the relative toxicity of the tuberculous process and compare it objectively with the resistance of the patient. It appears to be impossible to eradicate the entire disease. This fact and the paramount importance of the individual's resistance suggest that in a broad sense, tuberculosis should not be considered amenable to surgery.

**Further Experiences in Pulmonary Resection in the Treatment of Pulmonary Tuberculosis, Richard H. Overholt, Boston.**—This report dealt with the experience in 200 resections (192 patients), performed since 1934. The first ninety three were done before April, 1944, and the patients received general anesthesia and were placed in the conventional side position. The remainder, done since April, 1944, were done under local anesthesia and placed face down on the operating table. The objective has been to eliminate or at least minimize the occurrence of bronchopleural fistulas, empyema, and spreads. Fistulas are now quite rare. The patient is positioned on the table face down, to prevent the flow of secretions into the contra lateral lung. Local anesthesia is used, infiltrating the skin and the intercostal nerves. In the face down position, the patient breathes better, has a higher vital capacity than when lying on his side, and tolerates an open pneumothorax without positive pressure. An endotracheal tube is used routinely for aspiration. This series consisted of twenty resections for bronchial tuberculosis, thirty two for thoracoplasty failure, ninety four for extensive unilateral disease, twenty eight for extensive upper lobe disease, eighteen for basal disease, six for tuberculoma and two for giant cavities. Of these, 142 were previous treatment failures. The best results

were obtained in stabilized cases. The complications of lobectomy were fistula, empyema, wound infection, and spreads, both contralateral and ipsilateral, the latter being somewhat higher. There were more empyema and wound infections after pneumonectomy but fewer contralateral spreads. Late and delayed complications were less frequent after pneumonectomy than after lobectomy. Out of 127 pneumonectomies, forty-six were done on the right and eighty-one on the left side. Apical thoracoplasty accompanying an upper lobe resection reduces the likelihood of spread. It is important not to overstretch the remaining lung.

Dr. John Streider opened the discussion and said that the indications for lung resection in tuberculosis have not changed, and reported ten lobectomies (one operative death) for tuberculoma and apical cavity and thirteen pneumonectomies (two operative deaths) for basal cavities, extensive diseases, and thoracoplasty failures. Evidence of spread was noted after 60 per cent of the lobectomies and 45 per cent of the pneumonectomies. Resection does not appear to be the answer. Dr. E. J. O'Brien said that tuberculosis is an unpredictable and recurrent disease, and that it cannot be eradicated in toto surgically. Pneumonectomy is preferable to lobectomy insofar as it excises more of the disease. He emphasized that other forms of therapy have been successful, viz, thoracoplasty gives better results in extensive unilateral disease, and basal lesions are more often cured by measures other than resection. He thought that the face down position was excellent but stated that spreads do not result from the position on the table but from coughing. In combating tuberculosis, anything which augments the patient's immunity to the disease is important. One cannot operate on a constitutional disease, locally. Dr. Bailly, reporting eighty cases of pulmonary resection, said that his mortality was higher for pneumonectomy than lobectomy and that the incidence of spreads was proportional to the amount of sputum. Since complete aspiration of the bronchial tree is not possible, he urged the use of the Trendelenburg position to minimize spilling into the better lung. Dr. J. R. Head stated that in acute bronchial obstruction, which start early in the disease and are characterized by wheezing and difficult coughing, lobectomy was indicated, but that in all chronic bronchial obstructions thoracoplasty was effective. He added that he felt that 90 per cent of these resections were unnecessary, some other forms of therapy would have been more effective and safer. Dr. Sweet said, in closing, that he thought the results of resection had been better than he thought they would be. Dr. Overholt said with some emphasis, that he did not recommend resection generally; in fact, he rejected two out of three cases presented for resection. His aim is to salvage cases which appear to be hopeless with usual means of therapy. He restricts resections to those who have no apparent chance of recovery by any other means.

**Cavernostomy, F. C. Test, Detroit.**—This procedure consists of rib resection and drainage of a tuberculous cavity, which is entered with a cautery. The operation, which was described as "very messy," arrests rather than cures the underlying lesion. It is employed when other surgical procedures are not applicable. It is restricted to bad risks. This series covers seventy-four patients and eighty operations. They fall into three categories: (1) solitary large cavity without acute or progressive exudative disease, in patients with too limited a cardiorespiratory reserve to permit collapse therapy, (2) large, solitary cavity with minimal surrounding infiltration, located in the lower lobe, without active disease of the upper lobe, and (3) residual cavity beneath an optimal thoracoplasty collapse, in the absence of acute progressive exudative disease. As might be expected in such a group of salvage cases, morbidity and mortality were high, but the results in the second and third groups were sufficiently encouraging to warrant further use of cavernostomy in certain tuberculosis patients unsuited for other surgical procedures. The cavity is opened with a cautery and then packed; the wounds show a remarkable tendency to heal. There is sputum conversion in 78 per cent of the cases. Death is due to progression of the underlying lesion. The best results are in lower lobe cavities, where 83 per cent are arrested; in the postthoracoplasty group, 55 per cent were arrested. The worst results occurred where dyspnea was the outstanding symptom. Dr. W. A. Hudson pointed out the limitations of the operation but said that it tended to make the patient more comfortable and prolonged life. He advised that cavity drainage (Monaldi technique) be done first, and then cavernostomy, with use of a skin flap. Dr. W. L. Rogers also

endorsed the operation, especially for use in cavities in the upper portion of the lower lobe. He advised that it be done in stages and that the first step should be the preparation of a skin flap, which is later to be dropped into the cavity; packing the cavity is unnecessary.

**Surgical Removal of Foreign Bodies From the Heart.** Dwight E. Harken, Boston—This was a remarkable moving picture of three cases, showing the detailed technique of removing foreign bodies from the chambers of the heart. There were no deaths in a series of 134 operations for foreign bodies in the heart or pericardium. In one instance, it was only at the third attempt, and this at the request of the patient, that the foreign body was recovered from the right ventricle. More foreign bodies were left in situ than were removed. The question of removal often depends on the emotional reaction of the patient, who "harbors an unwelcome visitor in the citadel of his well being" (Grey Turner). The rationale of the removal of foreign bodies is based on the prevention of bacterial endocarditis (65 per cent of foreign bodies were infected), emboli, pericardial effusion, rupture or herniation of the heart, pain, and cardiac neurosis. Localization of foreign bodies in the right ventricle by x ray and fluoroscopy show them to lie anteriorly and apparently on the diaphragm. One third of the foreign bodies thought to be within the heart, were found to be elsewhere. Adequate exposure is essential. The bony cage of the chest is preserved by use of an incision through an intercostal space and division of costal cartilages, which are sutured when the chest is closed. A transpleural approach is used because it expedites the operation and improves the exposure. It is very important that the heart should be dislocated as little as possible from the position of maximum function. The heart, once exposed, should be kept moist and bathed in a novocain solution. Transfixion sutures are placed on either side of the proposed incision through the wall of the heart. After incision of the heart and removal of the foreign body with a hemostat, these sutures are crossed, until closure is effected with interrupted sutures, and this suture line is reinforced with a pericardial graft. The actual removal takes 15 to 25 seconds. The patient receives pressure transfusions during the operation to replace the blood loss which may amount to as much as a liter. In the discussion, the value of pressure transfusion and the transfixion sutures was emphasized. Dr. Decker pointed out that the length of survival was about the same whether the foreign body was removed or left behind, but that in many individuals, awareness of a foreign body in or around the heart produced marked emotional disturbances. Dr. P. C. Samson spoke of the safety of removal of these foreign bodies and the responsibility of determining whether they should be removed or left behind. Dr. Brodtkin told of a wounded soldier, exhibiting the signs of cardiac compression, who, when explored and when a thickened pericardial membrane was excised, was found to be harboring his dog tag in the pericardium. Dr. Miscal said that a foreign body left within the heart could produce symptoms of coronary thrombosis. He reported the removal of foreign bodies lying within the pulmonary artery, bronchi, and superior vena cava in thirty nine cases without any deaths. Dr. J. R. Head told of two cases of foreign body in the lung where the only symptom was hemorrhage, the surgical removal effected a cure. Dr. Claude Beck suggested that with intramural foreign bodies, mattress sutures be used to exteriorize them.

**Cardiac Resuscitation.** Mercier Fauteux, Boston—The usual methods of cardiac resuscitation (e.g., massage, adrenalin, electrical shock) employed after cardiac arrest (standstill) or primary ventricular fibrillation secondary to various causes, have not always been successful in reviving cardiac function after a brief period of complete stoppage of the circulation. After a very few minutes of standstill or ventricular fibrillation, the heart cannot be started again. The cause of failure of resuscitation may be (1) hyperirritability of the heart, (2) absence of cardiac tone, (3) elevation of the myocardial temperature, or (4) peripheral circulatory failure. The value of novocain, bromine chloride, cold solutions, and the intracardiac perfusions of glucose, Ringer's solution, and blood to control the causes of failure were investigated. These measures when properly employed and in conjunction with the usual methods, namely, artificial respiration, massage of the heart, and intracardiac injection of adrenalin, lessen considerably the incidence of failure. The first step in resuscitation should be to stop the ventricular fibrillation. In failure, hyperirritability may be augmented rather than lessened by too much massage or the too liberal use of adrenalin. The use of cold solu-

tions may be helpful by reducing myocardial temperature. Peripheral circulatory failure, a concomitant of cardiac standstill, is best combated by directly perfusing the heart. In the discussion, Dr. Claude Beck pointed out that, in evaluating experimental findings, a cat's heart will stop fibrillating spontaneously, while a dog's heart will not. He advocated the use of novocain and electric shock for resuscitation of the heart and said that this process was reversible until brain damage has been done. Dr. O. C. Brantigan and Dr. C. Crafoord told of cases of prolonged cardiac arrest in patients who were resuscitated by the use of novocain, massage, and adrenalin. Dr. Fauteux pointed out that not only cyclopropane but any anesthetic induction, when combined with the use of adrenalin, might throw the heart into fibrillation.

**Traumatic, Diaphragmatic Hernia.** Earle B. Kay, Memphis, Tenn.—Twenty-eight cases of traumatic hernias were reported; five were on the right side and twenty three on the left side. Seventeen of them were the result of perforating wounds and eleven, the result of contusions. Symptoms of acute obstruction developed in two cases while under observation, and resection of the colon was necessary in one patient, admitted with evidence of obstruction. These hernias were all repaired through a transpleural approach, which gave excellent exposure of both the abdominal and thoracic organs. The eighth or ninth rib was resected, and the phrenic nerve was crushed routinely. In only two of these hernias, were sacs present. The diaphragm was repaired with tantalum wire and the chest was closed without drainage except in the one instance which required resection of the bowel. Since there were many diaphragmatic injuries in the war, it seems probable that this condition will be seen more frequently in the future.

**Thoracogastric Fistula Caused by Surgical Mistreatment of Herniated Stomach.** G. E. Lindsag, New Haven, Conn.—Two cases were presented in which a herniated intrathoracic stomach had been inadvertently drained surgically (by other surgeons) under the misapprehension that a left pyothorax was the underlying condition. The first case developed a chronic peptic ulcer at the site of the previous catheter drainage, with erosion of the overlying rib and repeated hemorrhages from the intercostal artery. The treatment consisted of partial gastric resection, reduction of the herniated viscera, and repair of the diaphragm. In this case, the sac was adherent to the chest wall, and there was no pneumothorax or empyema. The second case presented a massive pyopneumothorax and gastric fistula, subsequent to a similar error in diagnosis. It was treated by thoracotomy for drainage, jejunostomy for feeding, and later reduction and repair of the herniated stomach. In both cases, definite history of previous chest trauma should have afforded an adequate clue to proper diagnosis and treatment. In view of the large number of men with chest wounds returning from the war in civilian life, attention should be called to the possibilities of incorrect diagnosis which might be made by the unwary, as well as to methods of handling complications following ill advised surgical intervention.

**Congenital Eventration of the Diaphragm: Surgical Management; Case Report.** Dewey Bisgard, Omaha.—Congenital eventration of the diaphragm is a rare condition; only 143 cases have been reported, for all ages. It is not a hernia but an abnormally high position of one leaf of the diaphragm, which may be paralyzed. They occur more frequently on the left side. It is rarely recognized and probably mistaken in some instances for other lesions which cause dyspnea and cyanosis in infants. The case was that of a 6 week old male baby, who was increasingly dyspneic and cyanotic from birth until at the time of operation; survival was possible only in an oxygen chamber. The eventration, which was right sided, was approached through the ninth interspace, and the diaphragm was found at the level of the second rib. Motion of the diaphragm appeared to be normal. The diaphragm was restored to its normal position by plicating and plication. The infant has remained well and developed normally up to the present, eighteen months after operation.

## Book Reviews

**Extensile Exposure Applied to Limb Surgery.** By Arnold L. Henry, M.B. Dublin; M. Ch (Hoo.), Cairo; F.R.C.S.I. Baltimore, 1915, Williams & Wilkins Company. \$7.

This book is an improvement over a similar book by the same author entitled *Exposure of Long Bones and Other Surgical Methods* published in 1920. As a surgical guide to selected areas of the extremities, it has no peers. Henry has described the exposures to those regions with which surgeons have had the greatest difficulty and the most complications. One can but wonder at the broad surgical experience and knowledge of anatomy which the author must possess. Not only is this book an excellent surgical text but it is also good literature.

In many instances it is necessary to expose not only bone but also nerves and blood vessels. The part of the title, *Extensile Exposures*, is well selected for the exposures described can be extended to include surgically important structures. Thus, each exposure may be likened to a main highway with many branching roads. The main highway is taken until the road leading to a particular destination is reached.

The anterolateral exposure of the humerus with its extension to include the contents of the axilla and neck is beautifully described. A posterior approach to the humeral shaft, to the radial nerve, and to the neurovascular bundle in the arm is demonstrated. Although this exposure is good for the humeral shaft, it is rather deep to the nerve and vessels and necessitates the splitting of muscle. The anterior approach to the radial shaft is one which is not used often enough. It is particularly adaptable to the upper third of the radial shaft, a region where surgical complications are frequent. The entire radius is available through this incision from the elbow to the wrist. The author's posterior approach to the structures in the buttocks is worthy of mention, for it avoids splitting the gluteus maximus as in some other approaches to this area. The sciatic nerve, the posterior portion of the acetabulum, and the posterior aspect of the neck of the femur may be exposed. The almost general applicability of the anterolateral incision to the shaft of the femur is widely accepted.

Many other approaches are described and these include back of the forearm, the hand, the knee and popliteal fossa, the back of the thigh and leg, the fibula and the peroneal nerve, the sole of the foot, and others. Description of all these exposures includes a detailed analysis of the anatomy and relations of the structures involved. Many other important details of surgical technique are given. These include pitfalls, the location of landmarks, the placement of incisions, the position of the patient on the operating table, and little practical tricks to find certain structures and to avoid others.

Everyone interested in surgery of the extremities could learn much of importance from this book.

### Books Received

The receipt of books is acknowledged in this section and this treatment must be regarded as sufficient acknowledgment of the courtesy of the senders. Selections will be made for more extensive review dictated by the interests of our readers and as space permits.

**A HISTORY OF MEDICINE.** By Douglas Guthrie, M.D., F.R.C.S. Cloth. Pp. 447, with 72 illustrations. Philadelphia, 1916, J. B. Lippincott Company.

**THE SURGICAL TECHNIC OF ABDOMINAL OPERATIONS.** By John L. Spivack, M.D., LL.D., Associate Professor of Surgery, University of Illinois. Cloth. Price \$10 Pp. 671, with 682 illustrations. Springfield, Ill., 1916, Charles C Thomas, Publisher.

**A TEXTBOOK OF GYNECOLOGY.** By Arthur Hale Curtis, M.D., Professor of Obstetrics and Gynecology, Northwestern University Medical School. Cloth. Price \$8. Pp 753, with 455 illustrations. Philadelphia, 1946, W. B. Saunders Company.

**AUTOPSY, DIAGNOSIS AND TECHNIQUE.** By Otto Saphir, M.D., Pathologist, Michael Reese Hospital and Professor of Pathology, University of Illinois Medical School. Foreword by Ludvig Hektoen, M.D. Cloth. Pp. 375, with 69 illustrations. New York, 1946, Paul B Hoeber, Inc.

**WOMEN IN INDUSTRY—THEIR HEALTH AND EFFICIENCY.** By Anna M. Baetjer, Sc.D., Assistant Professor of Physiological Hygiene, School of Hygiene and Public Health, The Johns Hopkins University. Cloth. Price \$4. Pp. 325, with 33 illustrations. Philadelphia, 1946, W. B. Saunders Company.

**DEMONSTRATION OF OPERATIVE SURGERY FOR NURSES** By Hamilton Bailey, F.R.C.S., Surgeon, Royal Northern Hospital, London. Cloth. Price \$5.50. Pp 337, with 530 illustrations. Baltimore, 1945, Williams & Wilkins Company.

**MEDICAL SERVICES BY GOVERNMENT.** By Bernhard J. Stern, Ph.D., Lecturer in Sociology, Columbia University. Cloth. Price \$1.50. Pp. 189, with no illustrations. New York, 1946, Commonwealth Fund.

**HUMAN TORULOSIS** By Leonard B. Cox, M.D., M.R.C.P., F.R.A.C.P., Lecturer in Neuropathology, Stewart Lecturer in Medicine, University of Melbourne, and Jean C. Tolhurst, M.Sc., Senior Bacteriologist to the Alfred Hospital, Melbourne. Cloth. Price \$2.50. Pp 137, with 67 illustrations. Melbourne, 1946, Melbourne University Press

**PERIPHERAL VASCULAR DISEASES.** By Edgar V. Allen, M.D., Division of Medicine, Mayo Clinic; Nelson W. Barker, M.D., Division of Medicine, Mayo Clinic; and Edgar A. Jones, Jr., M.D., Division of Medicine, Mayo Clinic. Cloth. Price \$10. Pp. 371, with 386 illustrations. Philadelphia, 1946, W. B. Saunders Company.

**ANESTHESIA IN GENERAL PRACTICE.** By Stuart C. Cullen, M.D., Head of the Division of Anesthesiology of the Department of Surgery, State University of Iowa Hospitals, Associate Professor of Surgery, State University of Iowa College of Medicine. Cloth. Price \$7.50. Pp 252, with 36 illustrations. Chicago, 1946, The Year Book Publishers, Inc

**MEDICAL EDUCATION AND THE CHANGING ORDER.** By Raymond B. Allen, M.D., Ph.D., Executive Dean, Colleges of Dentistry, Medicine and Pharmacy, University of Illinois. Cloth. Price \$1.50. Pp. 136, with no illustrations. New York, 1946, Commonwealth Fund

**NEW ASPECTS OF JOHN AND WILLIAM HUNTER** By Jane M. Oppenheimer, Bryn Mawr College. Cloth. Price \$6. Pp. 188, with 3 illustrations. New York, 1946, Schuman's

**THE NORMAL ENCEPHALOGRAM.** By Leo M. Davidoff, M.D., Professor of Clinical Neurological Surgery, Columbia University, and Cornelius G. Dyke, M.D., Late Associate Professor of Radiology, Columbia University. Cloth. Price \$5.50. Pp. 241, with 155 illustrations. Philadelphia, 1946, Lea & Febiger.

**THE PRINCIPLES OF NEUROLOGICAL SURGERY.** By Loyal Davis, M.S., M.D., Ph.D., D.Sc., Professor of Surgery and Chairman of the Division of Surgery, Northwestern University Medical School. Cloth. Price \$7.50. Pp. 532, with 313 illustrations. Philadelphia, 1946, Lea & Febiger.

**PENICILLIN, ITS PRACTICAL APPLICATION.** By Professor Sir Alexander Fleming, M.B., B.S., F.R.C.P., F.R.C.S., F.R.S., Professor of Bacteriology in the University of London, St. Mary's Hospital, London. Cloth. Price \$7. Pp. 359, with 59 illustrations. Philadelphia, 1946, The Blakiston Company.

**EARLY AMBULATION AND RELATED PROCEDURES IN SURGICAL MANAGEMENT.** By Daniel J. Leithausser, M.D., F.A.C.S., Chief of Surgery, St. Joseph's Mercy

Hospital, Detroit. Cloth. Price \$4.50. Pp. 232, with no illustrations. Springfield, Ill., 1946, Charles C Thomas, Publisher.

**TREATMENT OF BRONCHIAL ASTHMA.** By Vincent J. Derbes, M.D., Director of the Department of Allergy, Ochsner Clinic, New Orleans, and Hugo T. Engelhardt, M.D., F.A.C.P., Instructor of Clinical Medicine, Baylor University College of Medicine, Houston. Cloth. Price \$8. Pp. 445, with 61 illustrations. Philadelphia, 1946, J. B. Lippincott Company.

**RENAL HYPERTENSION.** By Eduardo Brown Menendez, Juan Carlos Fasciolo, Luis F. Leloir, Juan M. Munoz, and Alberto C. Taquini. Institute of Physiology, Faculty of Medical Sciences and Institute of Cardiology, V. F. Grego Foundation, Buenos Aires, Argentina. Translated by Lewis Dexter, M.D., Harvard Medical School. Cloth. Price \$6.75. Pp. 450, with 93 illustrations. Springfield, Ill., 1946, Charles C Thomas, Publisher.

**UROLOGIC ROENTGENOLOGY.** By Miley B. Wesson, M.D., Ex president of the American Urological Association. Cloth. Price \$5.50. Pp. 252, with 258 illustrations. Philadelphia, 1946, Lea & Febiger.

**STIMULATION OF HEALING WOUNDS AND ULCER PROCESSES.** Symposium edited and supplied with a foreword and summary article by Professor D. I. Goljberg. Cloth. Pp. 266, with 38 illustrations. U.S.S.R., 1946, Tomsk Medical Institute.

**OPERATIVE GYNECOLOGY.** By Richard W. TeLande, M.D., Professor of Gynecology, Johns Hopkins University. Cloth. Price \$18. Pp. 725, with 318 illustrations. Philadelphia, 1946, J. B. Lippincott Company.

**EXTENDED MYOMECTOMY AND OVARIAN CYSTECTOMY.** By Victor Bonney, M.S., M.D., B.Sc. London, F.R.C.S. England, Hon. F.R.A.C.S., M.R.C.P. London, Consulting Gynecological and Obstetric Surgeon to the Middlesex Hospital, London. Cloth. Price \$6.50. Pp. 232, with 242 illustrations. London, 1946, Paul B. Hoeber, Inc.

**THE AMERICAN HOSPITAL.** By E. H. L. Corwin, Ph.D., Executive Secretary, Committee on Public Health Relations of The New York Academy of Medicine. Cloth. Price \$1.50. Pp. 213, with no illustrations. New York, 1946, Commonwealth Fund.

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## Original Communications

### EXPERIMENTAL APPENDICAL PERITONITIS

#### II. THE SIGNIFICANCE OF IMBALANCE OF CIRCULATING FIBRINOLYTIC AND ANTIFIBRINOLYTIC FACTORS IN THE COURSE OF THE DISEASE

JOHN HOWARD KAY, M.D., AND JOHN SALEM LOCKWOOD, M.D.  
NEW HAVEN, CONN

*(From the Department of Surgery, Yale University School of Medicine)*

**T**HE preceding paper in this series<sup>1</sup> presented certain general observations regarding experimental appendical peritonitis in the dog

1 It is a disease of local origin which culminates in an acute toxemia characterized by profound disturbances in hemodynamic equilibrium and in impaired function of the liver, lungs, and other vital organs

2 The systemic character of the morbid response is reflected by shifts in the concentrations of many of the normal constituents of the blood, including water, electrolytes, nonprotein nitrogen, total protein, hemoglobin, and prothrombin

3 The outcome of the disease, regarding death or survival, appears to be related more to factors inherent in the "condition" of the animal prior to the experiment than to any demonstrable bacteriologic or anatomic variations in the character of the local lesions, as between dying and surviving animals.

4 The animals which survive tend to show no abnormality in prothrombin time immediately prior to the onset of the crisis of the disease, while those which succumb tend to enter the crisis of the disease already handicapped by an abnormal prothrombin time. Fluctuations in the amount of prothrombin, as measured by the Quick method, seem to coordinate in time with fluctuations in the sedimentation rate, the whole blood specific gravity, and the hematocrit

5. An attempt should be made to explain the correlation which seems to exist between the ability of individual dogs to survive the crisis of peritonitis and the stability, or reversibility, of their prothrombin levels

The present paper is a report of experiments designed to explore the possible relationship between survival from peritonitis and the antiproteolytic ac-

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tivity of the blood. This avenue of investigation was suggested by relevant inferences drawn from recent work of several investigators, particularly Tagnon, Ferguson, Christensen and MacLeod, and Grob.

Tagnon<sup>2</sup> demonstrated that the fall in blood pressure following the intravenous injection of trypsin is associated with prolongation in prothrombin time and an immediate reduction in the amount of circulating fibrinogen. Both of these reactions could be prevented by the preliminary administration of heparin. Tagnon inferred that the injected proteolytic enzyme converted prothrombin to thrombin, resulting in the intravascular conversion of fibrinogen to fibrin. The absence of formation of macroscopic clots was thought to be due to the fact that the fibrin was deposited as a dispersed film throughout the vascular tree and on the intima of blood vessels. Injection of thrombin caused the same reactions as trypsin, but heparin displayed no neutralizing effect on thrombin, as it did with trypsin.

More recently, Tagnon and his colleagues<sup>3</sup> have pointed out that serum of animals and patients in advanced shock frequently displays increased fibrinolysis and corresponding reductions in fibrinogen and prothrombin levels. Ferguson<sup>4</sup> and others<sup>5, 6</sup> have related the activity of a proteolytic enzyme to the normal blood-clotting mechanism, and have suggested that hemophilia is characterized by a deficiency of this factor.

Christensen and MacLeod<sup>7</sup> have described the properties of a naturally occurring proteolytic enzyme in human serum, which they call plasmin. The mechanism of streptococcal fibrinolysis is the activation of this enzyme by a product of the streptococcus, to which they assign the term streptokinase. In most respects the proteolytic enzyme system of serum is analogous to the proteolytic enzyme systems of the pancreas, trypsin, and chymotrypsin. Serum protease shows important qualitative and quantitative differences with trypsin, but the inhibitors of these two enzymes appear to be similar. Northrop's crystalline pancreatic trypsin inhibitor will inactivate serum proteolytic enzyme, but a larger amount of inhibitor is required in this reaction than is required when crystalline trypsin is employed.

Grob<sup>8, 10</sup> showed that the antiprotease activity of the serum of the rabbit could be substantially increased by the repeated administration to the animal of crude trypsin, either intramuscularly or by mouth. That induced increases in antiprotease activity were of potential significance in disease was supported by the fact that the size of the area of necrosis resulting from subcutaneous injection of trypsin, or of *Staphylococcus aureus*, was inversely proportional to the level of serum antiprotease activity. He confirmed the earlier observations of Wright,<sup>11</sup> and his colleagues, that bacterial growth was often related to the balance between proteolytic and antiproteolytic factors in the media, and showed further that sulfonamide action against *Staph aureus* was markedly reduced when proteolysis was dominant.<sup>12</sup>

A synthesis of the contributions of these investigators appeared to offer a new approach to an understanding of the basis for the morbid sequences in peritonitis. Tagnon and Ferguson had related abnormalities in the blood-

clotting mechanism, similar to those observed in peritonitis, with activation of a fibrinolytic factor in the blood; Christensen and MacLeod had clarified the relationship between fibrinolysis and serum protease activity and their respective inhibitors; and Grob had shown how an increase in the antitryptic activity of serum could be induced by prolonged administration of trypsin, and that augmentation of antitryptic activity had a definite bearing on the courses of at least two disease entities.

As an initial step in the investigation thus suggested, we have studied by relatively simple methods the fibrinolytic activity of the serum of dogs before and after the production of experimental peritonitis.

#### METHODS AND MATERIALS

Peritonitis was produced in dogs by ligation of the base of the appendix after freeing this structure from its blood supply. Castor oil was given immediately after operation, and supportive infusions of saline and glucose solution were given every twelve hours. (Full details on technique and management are given in the preceding paper.)

*Determination of Fibrinolytic Activity.*—We are using the term fibrinolytic activity as an expression of the *net balance* of the factors involved in the lysis of clotted fibrin, namely, the activated plasma proteolytic enzyme (the plasmin of Christensen and MacLeod) and the inhibitor of this enzyme, which has been described as being identical with pancreatic trypsin inhibitor.

Fibrinolytic activity was determined by two distinctly different techniques.

1 By simple incubation of recalcified oxalated dog plasma, at 37° C, determining whether spontaneous lysis of the dog's own fibrin occurred within a period of forty-eight hours. This determination is called serum fibrinolytic activity (SFA).

2 By adding to a standardized preparation of bovine fibrinogen some dog serum which has been treated with chloroform to remove at least a portion of the nonspecific inhibitor of proteolytic enzyme. This procedure (CSFA) permits the measurement of fibrinolytic activity under conditions in which no activity is demonstrable when only unmodified serum is used.<sup>13</sup> In our experiments it is complicated, however, by the fact that the bovine fibrinogen preparation contains a small amount of bovine fibrinolytic enzyme as an impurity.<sup>14</sup> Therefore, fibrinolytic activity as determined in this reacting system is compounded from the combined action of dog and bovine proteolytic factors, on the one hand, opposed by the dog antiproteolytic factor, on the other. In any quantitative expressions of CSFA, the value should, therefore, be considered more as a measure of the amount of proteolytic enzyme inhibitor than as a measure of the amount of the enzyme. An effort is being made to develop an improved technique which will more accurately measure the two factors independently.

Details of the technique employed for measuring SFA and CSFA follow.

*Serum fibrinolytic Activity (SFA).*—Blood was drawn from the jugular vein into a dry sterile syringe, then transferred to a sterile tube containing 0.5 c.c. of oxalate solution for each 10 c.c. of blood. The oxalate solution comprised

8 Gm. of potassium oxalate and 12 Gm. of ammonium oxalate, per liter. After centrifugation, the plasma was removed into sterile tubes. Plasma, 2 c.c., was placed in a small test tube, and four drops of 2 per cent  $\text{CaCl}_2$  solution added. Occasional samples failed to clot, a reaction which was not influenced by varying the amount of  $\text{CaCl}_2$  added (to be discussed later). If a clot formed, the specimen was placed in the water bath at  $37^\circ \text{C}$  and observed for fibrinolysis over a period of forty-eight hours.

*Chloroformed Serum Fibrinolytic Activity (CSFA)*—Serum was separated from clotted, recalcified plasma, prepared as described previously. One volume of chloroform was added to ten volumes of the serum, and the tube was shaken vigorously by hand for one minute. The tube was then placed in the water bath at  $37^\circ \text{C}$  for one hour, during which a precipitate formed in the lower (chloroform) layer. The specimen was then centrifuged and the supernatant was pipetted off the chloroform layer and placed in the refrigerator at  $4^\circ \text{C}$ . for about eighteen hours. The treated serum was then tested for fibrinolytic activity as follows. The serum, 2 c.c., was added to 0.1 c.c. of a solution of bovine fibrinogen\* containing 8 G mg. per cubic centimeter. To this was added 0.5 c.c. of distilled  $\text{H}_2\text{O}$  and, finally, 0.2 c.c. of bovine thrombin (200 units\*). The clotted specimen was placed in a water bath and observed for lysis. Lysis occurring in from zero to fifteen minutes was recorded as 4+; from fifteen minutes to one hour, 3+; from one hour to three hours, 2+; and from three hours on, 1+. A reading of 1- implies little fibrinolytic activity of the dog serum, because the bovine fibrin tended to undergo spontaneous lysis in six to ten hours when only saline solution was added.

*Fibrinogen determinations* were done by precipitating fibrin by the addition of calcium to plasma diluted with twenty volumes of 0.65 per cent sodium chloride solution. If a clot formed, it was collected on a glass rod, washed, and analyzed for nitrogen by the micro-Kjeldahl procedure. If only a flocculent precipitate formed, it was separated by centrifugation, and analyzed by the same method.

*Materials*—The materials used in these experiments were crystalline trypsin,† crude trypsin,‡ bovine fibrinogen and bovine thrombin,§ heparin|| in Putkin's menstruum, penicillin,¶ 200,000 units per cubic centimeter in beeswax and peanut oil (Romansky formula\*\*).

## RESULTS

In Table I are presented the results of determinations of SFA in a series of twenty-seven dogs, among which there were eleven deaths and seventeen survivals. Thirteen of these animals were subjected to several differing methods of treatment (to which detailed reference will be made later) and fourteen were controls. At this point it is desired to indicate only the relationship between

\*Supplied by Parke, Davis & Company, Detroit, Mich.

†Obtained from the Plant Research Laboratories, Bloomfield, N. J.

‡Obtained from Armour and Company, Chicago, Ill.

§Obtained from Parke, Davis & Company, Detroit, Mich., through the courtesy of Dr F.

A. Sharp.

||Supplied by Dr H. D. Shaner, Roche-Organon, Inc., Roche Park, Nutley, N. J.

¶Obtained from Dr C. F. Church of the Squibb Institute for Medical Research, E. R. Squibb & Sons, New York, N. Y.

\*\*Obtained from Dr C. F. Church of the Squibb Institute for Medical Research, E. R. Squibb & Sons, New York, N. Y.

TABLE I. SERUM FIBRINOLYTIC ACTIVITY IN DYING AND SURVIVING ANIMALS DURING COURSE OF DISEASE

DOG NUMBER	PROFIBR ACTIVITY	HOURS POSTOPERATIVELY						
		12	24	36	48	60	72	84
168 NT	-	-	+	No clot	Dead			
170 NT	-	-	+	Dead				
184 NT	+	+	-	+	No clot	Dead		
186 NT	-	+	No clot	Dead				
188 H	-	+	+	+	+	Dead		
190 H	-	-	-	+	+	+	Dead	
193 NT	-	-	-	-	-	-	+	Dead
196 T <sub>4</sub>	-	+	-	No clot	Dead	+		
197 T <sub>4</sub>	-	-	-	+		No clot	Dead	
207 P	+	+	+	Dead				
209 P	-	+	+	Dead				
172 NT	-	+	+	-	-	-	-	
174 NT	-	+	+	+	-	-	-	
176 NT	+	+	+	+	-	-	-	
178 NT	-	+	+	+	-	-	-	
180 NT	+	-	+	-	-	-	-	
182 NT	-	-	+	-	-	-	-	
192 NT	-	-	-	-	-	-	-	
194 NT	-	-	-	-	-	+	-	
195 T <sub>4</sub>	-	-	-	-	+	-	-	
198 T <sub>12</sub>	-	-	-	-	-	-	-	
199 T <sub>12</sub>	-	-	-	-	-	-	-	
200 T <sub>12</sub>	-	-	-	-	-	-	-	
201 P	-	-	-	-	-	-	-	
203 P	-	-	-	-	-	-	-	
205 P	-	-	-	-	-	-	-	
211 P	-	-	-	-	-	-	-	

NT, No treatment

H, Heparin

T<sub>4</sub>, Trypsin injections for four days

P, Penicillin

T<sub>12</sub>, Trypsin injections for twelve days

+, Complete lysis within forty-eight hours

-, No lysis, or incomplete lysis, within forty-eight hours

measurements of fibrinolytic activity and the course of the disease. The reactions were of two types:

*Failure of Clot Formation*—Table I indicates that in five instances the addition of calcium to the oxalated plasma failed to produce a clot. In these cases there developed, instead, a cloudy flocculent precipitate which dissolved in from ten seconds to five minutes. The amount of fibrinogen in these samples was usually greatly reduced. It cannot be stated definitely whether this failure of clot formation was due entirely to fibrinogenolysis or whether some other element in the clotting mechanism was at fault. Significantly, this type of reaction occurred only among the group of animals which died.

*Formation of a Clot, Followed by Spontaneous Lysis Within Forty-eight Hours*—The formation of a clot followed by spontaneous lysis within forty-eight hours occurred in at least one of the samples of blood taken from each of the eleven dogs which died. In four instances fibrinolysis occurred in the specimen collected twelve hours before one in which no clot formed upon addition of calcium. One or more positive tests occurred in eight of the sixteen animals which survived. However, in all but two of these the fibrinolytic activity was con-

TABLE II. FIBRINOGEN NITROGEN LEVELS\*

DOG NUMBER	PROPERA TITLY	HOUR POSTOPERATIVELY					
		12	24	36	48	60	72
193	104.0	93.5	99.4	67.4	112.9	112.0	127.1
196	54.6	50.4	74.7	24.2	Died	-----	-----
197	65.4	63.8	92.6	129.9	129.9	26.2	Died
154	67.9	95.0	94.0	120.7	71.6	126.0	120.3
176	94.4	95.4	101.1	107.1	49.9	99.0	Not done
178	108.0	37.0	111.5	153.0	128.8	150.8	162.8
192	77.0	84.6	123.1	90.2	110.3	111.7	123.0
194	61.8	82.0	43.7	45.4	39.8	118.0	142.4
195	37.2	78.6	119.8	115.3	113.6	84.2	93.8
198	27.7	70.0	76.4	11.0	99.4	60.6	93.5
199	88.7	119.2	115.0	117.5	86.4	119.4	113.0
200	77.2	103.5	113.8	114.4	104.8	91.6	103.2
Average	72.7	81.7	96.3	91.3	94.9	101.4	119.9

\*Expressed as nitrogen in milligrams per 100 cc. Abrogen =  $\times 6.25$

fined to the first thirty-six hours of the postoperative period. None of the samples from surviving animals showed fibrinolytic activity at seventy-two hours.

In Table II are depicted the values for fibrinogen nitrogen in blood samples collected at twelve-hour intervals from twelve of the dogs in this group. There was a wide variation between dogs in their preoperative fibrinogen nitrogen levels, and no very consistent trends in subsequent readings can be discerned. The two animals in this group which showed the "no clot" reactions (Dogs 196 and 197) both afforded very low fibrinogen nitrogen readings at that time. Attention is called to the remarkable lability of fibrinogen nitrogen levels in all of the animals. It is possible that this is due not so much to actual fluctuations in fibrinogen concentrations as to variations in the responsiveness of fibrinogen and prothrombin, in diluted oxalated plasma, to the addition of calcium, a potential source of error which is inherent in the method. Of some interest is the fact that average values of fibrinogen nitrogen appeared to be substantially higher after recovery from the disease than before its onset.

*Chloroform Serum Fibrinolytic Activity*—In Table III are presented determinations of fibrinolysis of clots compounded of bovine fibrinogen, bovine thrombin, and dog serum which had been treated previously with chloroform (simultaneous measurements of SFA are shown, for comparison). A reading of 1+ indicates that lysis occurred only after the period of time bordering on that required for lysis of bovine fibrin containing no added serum, and it is safe to infer that fibrinolytic and antifibrinolytic factors were at least in equilibrium with each other. The higher values, 2+, 3+, and 4+ indicate a relative lack of equilibration of these factors, due either to abnormally low antiproteolytic activity or to increased proteolytic activity. The data are arranged according to the stage\* of the disease in the individual animal as expressed by his general appearance, rather than according to strict chronology. This arrangement takes into account the considerable variations in the time of onset of the crisis of peritonitis.

\*The stages in the course of the experimental diseases are described in the preceding paper.<sup>1</sup>

TABLE III. CHLOROFORMED SERUM FIBRINOLYTIC ACTIVITY AND SERUM FIBRINOLYTIC ACTIVITY, IRRESPECTIVE OF THERAPEUTIC MEASURES

	DOG NUMBER	STAGE I PREOPERATIVE		STAGE II POSTOPERATIVE CRISIS		STAGE III RECOVERY FROM POSTOPERATIVE CRISIS		STAGE IV CRISIS OF PERITONITIS		STAGE V RECOVERY	
		CSFA	SFA	CSFA	SFA	CSFA	SFA	CSFA	SFA	CSFA	SFA
Died	209 P	3+	-	2+	+	2+	-	2+	+	Dead,	30 hr
	207 P	3+	+	2+	+	2+	-	3+	+	Dead,	36 hr
	197 T	4+	-	2+	-	2+	-	4+	+	Dead,	72 hr
	196 T	3+	-	2+	+	2+	-	4+	+	Dead,	48 hr
	193 NT	2+	-	1+	-	3+	-	3+	+	Dead,	84 hr
	190 H	2+	-	4+	-	3+	-	4+	+	Dead,	72 hr
	188 H	2+	-	4+	+	2+	-	4+	+	Dead,	60 hr
	192 NT	2+	-	1+	-	2+	-	1+	-	2+	-
Lived	194 NT	1+	-	3+	-	1+	-	3+	-	2+	-
	193 T	1+	-	2+	-	3+	-	3+	+	2+	-
	198 T	1+	-	2+	-	1+	-	1+	-	1+	-
	199 T	1+	-	1+	-	3+	-	2+	-	2+	-
	200 T	1+	-	1+	-	1+	-	1+	-	1+	-
	201 P	2+	-	2+	-	1+	-	1+	-	2+	-
	203 P	2+	-	1+	-	2+	-	2+	-	1+	-
	205 P	1+	-	2+	-	2+	-	2+	-	1+	-
	211 P	2+	-	2+	-	2+	-	2+	-	1+	-

Therapy indicated by P, penicillin, T, Trypsin for four days T<sub>12</sub> Trypsin for twelve days, H, heparin, NT, no treatment

CSFA, Chloroformed serum fibrinolytic activity

SFA, Serum fibrinolytic activity

\*These animals never seemed to recover from the postoperative crisis but moved directly from Stage II to Stage IV.

It is noted that the levels of CSFA were substantially higher, on the average, in the animals which died than in the animals which survived. All of the six animals with 1+ readings before operation ultimately survived, while the four animals with preoperative readings of 3+ and 4+ succumbed. At the crisis of the disease (Stage IV) six out of seven of the dogs which later died showed values of CSFA of 3+ or 4+, while, in the surviving group, only two out of ten were higher than 2+. Thus, a correlation does appear between the CSFA and the trend toward death or survival. Of greatest significance is the suggestion that this measurement served even before operation to distinguish one group of animals which was able to overcome the disease from another group which succumbed.

*Trypsin Administration.*—Reference has already been made to Grob's demonstration of the influence of trypsin administration upon the level of the antiproteolytic factor in the blood. If the level of antiproteolytic factor in the blood has a bearing on the resistance of the dog to experimental peritonitis it should be possible to establish this by preoperative administration of trypsin to a group of animals. The results of such experiments are shown in Tables IV and V. The intramuscular injection of 20 mg of crystalline trypsin for only four days proved to be insufficient to obtain consistent reduction in the level of antiproteolytic activity, as estimated by the CSFA (Table IV). Only one of these three dogs survived, and it happened to be the one with a 2+ reading before operation. Three additional dogs were, therefore, given similar injections of trypsin for twelve days, until the level of CSFA was 1+ in each. These three dogs all survived, and in them the course of the disease was notably modified from that in

TABLE IV FIBRINOLYTIC ACTIVITY DURING PERITONITIS; TRYPSIN INJECTIONS FOR FOUR DAYS AND TWELVE DAYS PREOPERATIVELY

DOG NO	DAYS PREOPERATIVE TRYPSIN	PREOPERATIVE CSFA SFA		POSTOPERATIVE HOUR							
				12		24 TO 36		48		72	
				CSFA	SFA	CSFA	SFA	CSFA	SFA	CSFA	SFA
195	4	2+	-	2+	-	3+	-	3+	+	2+	-
196	4	3+	-	2+	-	4+	+	Dead			
197	4	4+	-	2+	-	3+	+	4+	+	Dead	
198	12	1+	-	2+	-	2+	-	1+	-	1+	-
199	12	1+	-	1+	-	1+	-	1+	-	2+	-
200	12	1+	-	1+	-	1+	-	1+	-	1+	-

three simultaneously studied controls, all of which died. None of the trypsin-injected animals showed signs of collapse at any time; they continued to eat and drink and respond to attention. Unfortunately our supply of crystalline trypsin was then exhausted, no more could be obtained, and it became necessary to resort to a different method of trypsin administration.

Twelve dogs were fed 500 mg of crude trypsin daily for six days. The trypsin was placed in a capsule and the animal was forced to swallow it under observation. Measurements of SFA and CSFA in three of the dogs afforded indirect confirmation to Grob's observation that the feeding of trypsin would bring about an even more prompt rise in antiproteolytic factor than that produced by injection of the enzyme (Table V). Eleven of the twelve animals so

TABLE V FIBRINOLYTIC ACTIVITY DURING FEEDING OF TRYPSIN (500 MG. CRUDE TRYPSIN IN GELATIN CAPSULE DAILY)

DOG NUMBER	DAY OF FEEDING					DAY OF OPERATION (CSFA)
	1 SFA	2 SFA	3 SFA	4 SFA	5 SFA	
213	-	-	+	+	-	1+ (Survived)
214	-	+	+	-	-	1+ (Survived)
215	-	+	-	-	-	1+ (Survived)

prepared survived. This was strictly a survival experiment, and detailed measurements of fibrinolytic activity were made in only the three animals depicted in Table V. However, the low mortality rate pointed in the same direction as had the experiment with trypsin injections. Although all but one of the trypsin-fed dogs survived, they did appear acutely ill, and went through a definite disease crisis, in contrast with the three animals which were given trypsin by intramuscular injections and who showed almost no reaction to the disease.

There were, thus, a total of fifteen animals to which trypsin had been given in amounts either demonstrably or presumably sufficient to cause a significant rise in the level of antiproteolytic factor (Table VI). Only one of these fifteen

TABLE VI INFLUENCE OF PREOPERATIVE TRYPSIN ON MORTALITY OF PERITONITIS IN DOGS

ROUTE	DURATION (DAYS)	NUMBER OF DOGS	SURVIVED	DIED	MORTALITY (%)
Intramuscular	12	3	3	0	0
Oral	6	12	11	1	8.3
Total		15	14	1	6.6
Controls		91	53	38	41.7

animals died from peritonitis. This mortality of 6.6 per cent contrasts favorably with the mortality rate of 41.7 per cent in the ninety-one control animals discussed in the preceding paper.\*

*Penicillin Treatment.*—Reference was made in the preceding paper to the work of Fauley, Duggan, Stormont, and Pfeiffer,<sup>14</sup> who claimed to have demonstrated a significant protective effect with penicillin to the treatment of an experimental disease presumably identical with that employed in our work. They reported a mortality of 92.6 per cent in twenty-seven controls, and no mortality from peritonitis among dogs treated with penicillin, particularly when the drug administration commenced immediately after the operation. However, they excluded from the experimental series twenty-eight animals which died of an internal fecal fistula and four which died of postoperative bronchopneumonia. Recalculation of their data indicates that the over-all mortality of penicillin-treated animals was more nearly 50 per cent, when deaths from all causes were included. In our own experiment the mortality rate among ninety-one control animals was 41.7 per cent, approximately one-half the figure obtained by the Naval investigators. The reason for this difference is not apparent, but it could be related to differences in the types of dogs available, or to the factor of climate, or laboratory temperature.

In an effort to evaluate penicillin treatment under the conditions of our own experiments, peritonitis was produced in fifteen dogs by the standard technique, and injections of penicillin were added to the other measures employed in post-operative care. Each dog was given injections of 50,000 units of penicillin in 0.25 c.c. of the beeswax-peanut oil mixture, commencing immediately after the operation and repeated every twelve hours for five days, so that each dog received 500,000 units of penicillin, a relatively large dose. Random samples of blood were collected for penicillin assay from three of the dogs at various times and the values showed a range of variation from 0.03 units to 1.2 units per cubic centimeter. The number of these determinations was not sufficient to provide any basis for correlation between penicillin level and survival.

Ten of the fifteen animals which were treated with penicillin survived. In Table VII are depicted the results of fibrinolytic studies in six of the animals.

TABLE VII FIBRINOLYTIC ACTIVITY DURING PERITONITIS; TREATMENT WITH PENICILLIN

DOG NUMBER	PREOPERATIVE		POSTOPERATIVE HOUR							
			12		24		48		72	
	CSFA	SFA	CSFA	SFA	CSFA	SFA	CSFA	SFA	CSFA	SFA
201	2+	-	1+	-	2+	-	1+	-	1+	-
203	2+	-	1+	-	1+	-	2+	-	1+	-
205	1+	-	1+	-	2+	-	1+	-	1+	-
207	3+	+	2+	+	3+	+	Dead		-----	
209	3+	-	2+	+	3+	+	Dead		-----	
211	2+	-	2+	-	2+	-	2+	-	1+	-

\*By the time this article was published an additional nine pairs of dogs had been studied, one animal of each pair was prepared with daily injections of a solution of crude trypsin for twelve days and the other served as a control. There were seven survivors and two deaths in the trypsinized group, and four survivors and five deaths in the control group. If these are added to the three pairs in the crystalline trypsin series the mortality rate in the trypsin-injected group becomes 16.6 per cent, and in the paired control group, 66.6 per cent, with twelve animals in each. If all of the trypsinized animals are pooled together the mortality rate of the combined series of twenty-seven animals is 21.1 per cent. The last series of experiments with crude trypsin was performed by Dr. Donald G. C. Clark, and will be reported in detail later.



including four dogs which survived and two animals which died. (These data are also included in Table III.) It is noted that the two penicillin-treated animals which died were those which displayed increased fibrinolytic activity of chloroformed serum before operation.

The results in this limited series of fifteen animals fail to demonstrate any specific protective action by penicillin administered by the technique employed. It is possible that a higher survival rate would have been afforded by giving the penicillin every four hours, as Fanley and his colleagues used it. However, Romansky<sup>15</sup> showed that the beeswax and peanut oil vehicle maintains levels of penicillin for eighteen to twenty-four hours, this, coupled with the fact that we gave at least twice as large a total dosage of the drug as the other workers, makes it unlikely that our results were due to inadequate penicillin treatment.

*Heparin Treatment*—Since Tagnon had shown that the reaction to intravenously injected trypsin was modified in heparinized animals, the influence of heparinization on the course of peritonitis was determined in five dogs. The dogs were injected with a single dose of 200 units of heparin in Pitkin's menstruum<sup>16</sup> twelve hours after the operation. The clotting time was maintained above ten minutes for about forty-eight hours. None of the animals survived, the deaths occurred at between 60 and 216 hours following the operation. One factor in the deaths may have been the formation of large hematomas at the sites of the heparin injections.

The SFA in the heparinized dogs appeared to be increased (Table I, Dogs 188 and 190) and these animals, as a group, showed more profound degrees of hemolytic anemia than most of the controls.

On the basis of these discouraging results it was decided that heparin offered no promise as a therapeutic agent in peritonitis, and the work with anti-coagulants was abandoned.

#### DISCUSSION

In the preceding paper it was suggested that survival from this type of experimental peritonitis is largely determined by factors inherent in the makeup of the animal at the time the operation is performed. The normality of the prothrombin time leading during the period of recovery from the immediate effects of the operation afforded a significant basis for prognosis concerning the outcome. In the present paper a correlation has been drawn between survival and the balance of factors concerned in the mechanism of fibrinolysis. Animals which happen to possess a sufficiently high titer of antifibrinolytic factor in the blood, or in which this titer is raised by preliminary administration of trypsin, appear to be best prepared to withstand the deleterious effects of appendiceal gangrene and peritonitis. The evidence further suggests a correlation between the fibrinolytic-antifibrinolytic equilibrium and the phenomena of erythrocyte sedimentation, intravascular hemolysis, intravascular fibrinolysis, and reduced activity of prothrombin.

These observations offer a new concept of the basis for some of the morbid physiologic processes in peritonitis, and perhaps in other diseases characterized

by a similar shock phase. The evidence is not yet available to indicate what factor in the disease process is ultimately responsible—whether it is the absorption of specific or nonspecific bacterial proteins, the absorption of products of tissue autolysis, or a functional derangement of the liver. Much more work will be needed before this aspect of the subject can be clarified.

Before concluding the discussion, mention should be made of the publications of Kusely and Bloch,<sup>18</sup> of Smith and Smith,<sup>19</sup> and of Mirsky and Freis<sup>20</sup> which indicate a broader field of application of the phenomena under consideration.

Kusely and Bloch<sup>18</sup> have studied the physical pattern of blood flow in the small vessels and capillaries of the aqueductum or conjunctiva during the crisis of experimental malaria in monkeys and after severe thermal burns in dogs. In the terminal phases of these diseases the erythrocytes show a tendency to form into coagulated cords and masses of cells, and the leucocytes tend to adhere to the vascular intima. Marked hemoconcentration and stasis of blood are demonstrable in the capillaries and vessels. Kusely referred to this process as sludge disease. He believed that the initial occurrence leading to sludge formation is the deposition upon erythrocyte surfaces of a sticky film, presumably a fibrinogen derivative which not only tends to cause adhesion of the cells to one another, but also facilitates the engulfment of the cells by the fixed macrophages. The breaking up of sludge which may occur rapidly following the institution of effective treatment, is likely to be followed by greatly accelerated destruction of red cells. The observations on peritonitis presented in this paper are compatible with the view that sludge formation occurs in the advanced stages of this disease as well and that the sticky film to which Kusely refers might be a product of the action of a proteolytic enzyme upon fibrinogen or prothrombin. There already exists strong support for the view that the sequence of clotting may be initiated through action of a proteolytic enzyme.<sup>4</sup>

Smith and Smith<sup>19</sup> have demonstrated a fibrinolytic principle in the menstrual discharge, and in the blood of menstruating and eclamptic women, which is highly toxic for small animals. This principle appears to be identical with the "necrosin" which Menkin has prepared from sterile inflammatory exudates. The menstrual toxin can be neutralized by an antifibrinolytic factor which Smith and Smith have found in the globulin fraction of normal plasma protein. This work is cited as additional evidence of the possible significance in other diseases of a disturbance in the equilibration of proteolytic and antiproteolytic factors in animal metabolism.

Mirsky and Freis<sup>20</sup> have suggested, on essentially theoretical grounds, that a proteolytic enzyme may be released or activated when extensive destruction of animal tissues takes place, and that this enzyme "in turn may be responsible not only for changes at the site of injury, but also for the production of catalytic factors whose effect may be reflected in renal, hepatic, and other systemic and functional depressions." An investigation of the influence of antiproteolytic factors upon the phenomenon of increased protein catalolism during acute infection, and after severe trauma, is now in progress in this laboratory.

## SUMMARY AND CONCLUSIONS

1. Experimental peritonitis has been produced in 128 dogs, and a search has been made for the factors of greatest significance in determining the outcome of the disease. Preliminary studies in ninety-one control animals have already been reported. This paper concerns an investigation of the significance, in respect to survival, of the balance of fibrinolytic and antifibrinolytic factors in the blood of thirty-seven animals.

2. Evidence of spontaneous lysis of plasma fibrinogen and fibrin occurred with much greater frequency in eleven animals which died (one not measured) than in sixteen animals which survived (nine not measured). Lysis invariably occurred in samples drawn within twelve hours preceding death.

3. Sharp fluctuations in available fibrinogen nitrogen were observed during the course of the disease in all of the animals. The correlation between fibrinogen nitrogen levels and the activity of fibrinolytic factors is not clearly established. Animals which survive show levels of fibrinogen nitrogen approximately 65 per cent greater than preoperative values.

4. The fibrinolytic activity of chloroform-treated serum was significantly higher in dogs which died than it was in dogs which survived.

5. The preoperative administration of trypsin in amounts sufficient to build up the antiproteolytic activity of the serum had a significant influence on survival. Only one of fifteen animals so treated died, which contrasts with a mortality rate of 41.7 per cent in the ninety-one control animals.

6. Neither penicillin nor heparin were of therapeutic value in experiments on small groups of dogs.

7. Some of the literature which bears on this subject is reviewed, and certain of the implications of these results are discussed.

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## COEXISTENT DUODENAL ULCER AND GASTRIC MALIGNANCY\*

ALBERT FISCHER, M.D.,† O. THORON CLAGETT, M.D.,‡ AND  
JOHN R. McDONALD, M.D.,§ ROCHESTER, MINN.

**M**EDICAL literature concerning the pathology of the stomach and duodenum is voluminous. It is surprising, however, that references in the literature to the coexistence of malignant lesions of the stomach and duodenal ulcer are very rare. A discussion of this subject was not encountered in any of the textbooks of pathology which were consulted.

### REVIEW OF THE LITERATURE

Easterman and Balfour<sup>1</sup> stated that " . . . in contrast to gastric ulcer which presents the diagnostic and prognostic problem attributable to the ever-present menace of actual or potential carcinoma, the presence of duodenal ulcer is in a certain sense an insurance against gastric carcinoma."

Boekus<sup>2</sup> wrote "I have found that duodenal ulcer patients with marked gastric hyperchlorhydria and hypersecretion rarely die of gastric carcinoma. I have been in the habit of attempting to dispel a cancer phobia in patients with duodenal ulcer by stating that in my experience patients with this disease are much less likely to develop cancer of the stomach than those who have had no stomach disease whatever."

Smithies and Ochsner<sup>3</sup> had twelve patients in whom gastric carcinoma was coexistent with benign peptic ulcer, in eight of whom the peptic ulcer was in the duodenum.

Wilbur and Rivers<sup>4</sup> in 1932 published a statistical study of thirty-three cases of associated cancer of the stomach and duodenal ulcer which had been encountered at the Mayo Clinic up to that time. They found that the carcinoma of the stomach was the outstanding lesion in all except four of the cases. All of the various types of carcinoma of the stomach were represented in this group. In the group of thirty-three patients, nineteen had active duodenal ulcers, six had perforating or subacute duodenal ulcers, and seven had healed duodenal ulcers. In ten cases the duodenal ulcer was an incidental lesion, that is, it was not suspected before operation or post-mortem examination. There were three cases in which achlorhydria was present and in all three the carcinoma was inoperable. In nine cases the free acid content of the gastric juice was fifty or more. Four patients had undergone gastroenterostomy previously, and one had undergone excision of the duodenal ulcer and pyloroplasty. These authors were able to divide their cases into three groups: those in which the history was definitely that of ulcer, those in which the history was fairly definitely that of

ulcer, and those in which there were no characteristics suggesting the presence of peptic ulcer.

In 1938 Purvis and Jaffe<sup>11</sup> published a report of 2471 roentgenographic examinations performed at the Cook County Hospital in Chicago. In the large group of patients a total of 477 were found to have peptic ulcer. Of these, 240 patients had gastric ulcers, 235 had duodenal ulcers, and 2 had jejunal ulcers. No eleven of these patients had both gastric and duodenal ulcers. None of the patients was said to have a duodenal ulcer associated with a gastric malignant lesion.

Kosterian and Halfour<sup>12</sup> stated that of 1548 patients undergoing roentgenologic examination of the stomach because of digestive disturbances, 2017 (128 per cent) had deformities of the duodenal cap characteristic of duodenal ulcer. Of these patients, 167 (8 per cent) had roentgenologic evidence of gastric ulcer. In twenty-four cases evidence of both duodenal and gastric ulcers was found. None of these patients was said to have a duodenal ulcer associated with a gastric malignant lesion.

Christiansen<sup>13</sup> reported the gastroscopic findings in seventy cases of roentgenologically verified duodenal ulcers. In forty-nine of these cases he demonstrated definite changes in the gastric mucous membrane. In twenty-one cases the gastroscopic findings were normal. In the forty-nine cases the pathologic changes noted were as follows: gastritis chronic superficial, thirty-four cases; gastritis chronic hypertrophic, eight cases; gastritis atrophic, one case; erosion in normal stomach, five cases; erosion in abnormal stomach, three cases; polymucous hemorrhages in normal stomach, one case. Christiansen apparently did not find any cases in which a duodenal ulcer was associated with a gastric malignant lesion.

### PRESENT STUDY

Our interest in the study of coexistent duodenal ulcer and gastric malignant lesions was stimulated by seeing at operation a patient whose clinical course strongly suggested the presence of both lesions. Data concerning this patient will be presented with those of others later.

The material for study consisted of records of forty-eight patients having proved coexistent lesions seen at the Mayo Clinic between June, 1911, and January, 1947, inclusive. The criterion for the presence of a duodenal ulcer was the observation of the ulcer at operation or necropsy. The roentgenographic demonstration of a duodenal ulcer was not considered as sufficient evidence for its presence. It is also a fact that when resection of the stomach is performed, a duodenal ulcer is rarely excised, therefore, surgically removed material was of little value in demonstrating or excluding the presence of a duodenal ulcer. The carcinoma of the stomach was verified histologically, except in four cases in which the tissue was not available for study. However, these patients had lesions which at operation appeared to be carcinoma and they had died within short periods after operation, apparently of carcinoma of the stomach. The microscopic diagnosis of a malignant lesion was based on universally accepted criteria. Epithelial atypia and similar regenerative phenomena about the margins of otherwise benign gastric ulcers were not considered indicative of

carcinoma There were twelve additional cases in which a presumptive diagnosis of duodenal ulcer and of gastric malignant lesion was made. However, the records in these cases lacked adequate information to satisfy the foregoing criteria For example, there may have been roentgenologic evidence of both lesions but surgical exploration was not performed.

*Incidence.*—The forty-eight patients were seen at the Mayo Clinic between June, 1911, and January, 1945, inclusive. During this time approximately 13,000 patients who had carcinoma of the stomach and approximately 45,000 patients who had duodenal ulcer were seen Approximately 600 patients who had co-existent duodenal ulcer and gastric ulcer were seen during the same interval. Basing an estimate on these figures, it is seen that coexistent duodenal ulcer and gastric malignant lesion occur very rarely. Of the patients having duodenal ulcer, seen at the clinic during this time interval, 1 in 938 (0.1 per cent) had a coexistent gastric malignant lesion It is difficult to estimate accurately the incidence of duodenal ulcer in the general population. If one accepts the frequently quoted figure of 10 per cent, then the incidence of the coexistent lesions would be about 0.01 per cent in the general population.

The average age of these forty-eight patients was 52.9 years Three were between 30 and 40 years, sixteen between 40 and 50 years, sixteen between 50 and 60 years, eleven between 60 and 70 years, and two between 70 and 80 years. The youngest was 32 and the oldest was 78 years of age. This age range is about the same as that of carcinoma of the stomach in general

Of the forty-eight patients, thirty-nine were men and nine were women This also coincides with the relative occurrence of carcinoma of the stomach in the two sexes

The duration of symptoms referable to lesions in the stomach and duodenum varied from three days to forty-six years Among the patients who stated the duration of their symptoms, the average length of time was 11.3 years

The gastric acidity levels among the forty-eight patients showed a wide range of variations There did not appear to be any correlation between the degree of gastric acidity and the nature of the peptic lesions After Ewald test meals, determinations of gastric acidity fell into the following groups: total hydrochloric acid of 50 or more, nineteen patients; total hydrochloric acid between 25 and 50, nineteen patients; total hydrochloric acid less than 25, six patients, free hydrochloric acid absent after Ewald meal, two patients Determinations of gastric acidity were not made in two cases.

The average hemoglobin level for the group was 12.05 Gm per 100 c.c. of blood The lowest hemoglobin level was stated to be 20 per cent of normal and the highest was 17.4 Gm per 100 c.c. of blood

Roentgenologic examinations were carried out in forty-six of the forty-eight cases. The diagnosis of coexistent gastric and duodenal lesions was made in twenty-two of the forty-six cases. The filling defect in the stomach was definitely stated to be due to carcinoma in sixteen of the twenty-two cases The gastric lesions were not visualized in five of the forty-six cases and the duodenal ulcers were missed in eleven cases. The various roentgenologic diagnoses were as follows: carcinoma of the stomach and duodenal ulcer, sixteen cases; gastric

ulcer and duodenal ulcer, six cases; carcinoma of the stomach, seven cases; gastric ulcer, five cases; duodenal ulcer, three cases; pyloric obstruction, one case; lesion at outlet of stomach, two cases; prepyloric lesion, one case; hypertrophic gastritis and duodenal ulcer, two cases; obstruction of the lower part of the esophagus, deformity of cardia, one case; negative, two cases.

Among the forty-eight cases considered in this study, there were four instances of previous operation on the stomach or duodenum. These procedures were as follows: Heineke-Mikulicz pyloroplasty with excision of the duodenal ulcer (carcinoma of stomach thirteen months later); excision of duodenal ulcers on anterior and posterior walls and pyloroplasty (carcinoma of stomach nine years later); posterior gastroenterostomy and appendectomy (carcinoma of stomach ten months later); emergency closure of perforated peptic ulcer (carcinoma of stomach eighteen months later).

*Pathologic Findings.*—It is difficult to evaluate the nature of the duodenal ulcers in the majority of these cases, because in most instances no tissue was removed from the region of the ulcer for microscopic study. From the surgical descriptions one would assume that the majority of the duodenal ulcers were healed lesions or scars at the time of operation. In only four cases were the duodenal ulcers described as subacute or perforating lesions. The fact that most of the duodenal ulcers were inactive is perhaps significant in that they may have been modified by the presence of the superimposed gastric lesions. In the tissues obtained at post-mortem examination, evidence of duodenal ulcers consisted of scars in two cases, and one chronic duodenal ulcer.

The gastric lesions were predominantly carcinomas. There were one lymphosarcoma and one unclassified high-grade malignant lesion. As previously stated, there were four cases in which the gastric lesions grossly appeared to be carcinomas and were inoperable. No tissue was removed for microscopic study. In each of these four cases the patient died within a short time as a result of what appeared to be extensive carcinoma of the stomach. In the remaining forty-two cases all types of carcinoma of the stomach were represented. In twenty-nine of the forty-two carcinomas the lesion was ulcerating. By Broders' method of grading, the carcinomas were divided as follows: adenocarcinoma, grade 4, ten cases; adenocarcinoma, grade 3, thirteen cases, adenocarcinoma, grade 2, sixteen cases; adenocarcinoma, grade 1, two cases, adenocarcinoma, grade 1, in an adenoma, one case.

The malignant lesions were encountered most frequently along the lesser curvature of the stomach in this group of cases. There did not appear to be any correlation between the nature of the lesion and its location in the stomach. The distribution of the various lesions was as follows: prepyloric region or antrum, eleven cases; lesser curvature, seventeen cases; diffuse involvement, six cases, posterior wall, nine cases; cardiac portion, two cases; anterior wall, one case; greater curvature, one case; microscopic diagnosis of carcinoma associated with diffuse hypertrophic gastritis, one case.

*Signs and Symptoms Referable to the Stomach and Duodenum.*—In this group of forty-eight cases of coexistent duodenal ulcer and gastric malignant



lesion there were twenty-nine cases in which there were fairly typical symptoms of peptic ulcer preceding the discovery of the malignant lesions by five years or more. In ten cases the symptoms were apparently initially those of carcinoma of the stomach. In the remaining nine cases it was difficult to decide whether the symptoms initially were due to the gastric lesions or to the duodenal ulcers. However, since the majority of the duodenal ulcers were inactive or healed lesions, one would assume that the duodenal ulcers probably preceded the gastric lesions in practically all of the cases.

It was possible to divide the cases in this study into the following four groups according to the nature, progression, and duration of the symptoms. (1) cases in which there was a definite change in the character of symptoms, twenty-four; (2) cases in which there was a change in the degree of severity of the symptoms, fifteen; (3) cases in which the symptoms were progressive, seven; (4) cases in which no changes in the symptoms were noted, two.

It is significant that in this group of patients, the majority of whom suffered from dyspepsia, presumably due to duodenal ulcers, for relatively long periods, only twenty-four noticed a definite change in the character of the symptoms. In this group the changes in the character of the symptoms included one or more of the following: (1) diminution of the relief obtained by taking alkalies or eating food; (2) cessation of periodicity of the abdominal distress or pain, these symptoms becoming more nearly constant than they had been; (3) shift in the location of the pain or the extension of the pain; (4) sensation of rapid filling of the stomach; (5) hemorrhage; (6) abdominal tenderness; (7) palpable abdominal mass.

*Survey of Subsequent Course*—It was possible to obtain a follow-up record of forty seven of the forty-eight patients in this study. Twelve patients were alive more than five years after the diagnosis of coexistent duodenal ulcer and gastric malignant lesion was made, two of the twelve patients being alive twenty and twenty-one years, respectively, after this diagnosis had been established. Of the patients who died, seven died while in the hospital and twenty-two died of gastric malignant lesions at varying intervals.

#### COMMENT

Although duodenal ulcer and gastric carcinoma are of common occurrence, their coexistence is rare. It is possible that in the presence of carcinoma of the stomach, a duodenal ulcer may be easily overlooked, however, this group of cases demonstrates that the symptoms are usually of long duration and that one would be inclined to search carefully for a benign lesion in the duodenum or stomach. In a number of cases the diagnosis of duodenal ulcer had been established previously and in the majority of the more recent cases both the gastric and the duodenal lesions were demonstrated by the roentgenologist preoperatively.

It has been observed by other workers<sup>1, 2, 4</sup> that a patient who has a duodenal ulcer has relatively good assurance that the likelihood of carcinoma of the stomach developing is rather slight. The clinical data and pathologic specimens in these cases were studied carefully in an effort to determine whether the con-

ditions associated with these duodenal ulcers differed from those of duodenal ulcers in general. It was thought that perhaps hyperchlorhydria or even the bland diet might afford protection against gastric carcinoma for the usual patient having a duodenal ulcer. However, as previously stated, the gastric acidity levels in this group of cases showed wide variation and many of the patients had been under careful medical management. There was no correlation between the gastric acidity and the type or location of the malignant lesion. No conclusion was reached as to why patients who have duodenal ulcers rarely have gastric carcinoma.

It is significant that many of the duodenal ulcers in this series of cases were inactive or healed at the time of operation. Perhaps the development of the gastric lesions produced alterations which tended to heal the duodenal ulcers. Levels of gastric acidity prior to the development of the gastric lesions were not known in most instances. It is possible that in some cases the gastric acidity was decreased as a result of the superimposed gastric lesions.

It is of interest that the survival rate in this group of cases was considerably higher than that usually found in cases of carcinoma of the stomach. It was felt that this was due to the fact that many of the malignant lesions were discovered early. Perhaps patients who have duodenal ulcer are "stomach conscious" and are likely to consult a physician earlier than the average patient who has carcinoma of the stomach.

The symptoms and signs referable to the stomach and duodenum in this group of cases have already been discussed. It is noteworthy that only twenty-four of the forty-eight patients were able to detect a change in the character of their symptoms when the gastric lesions became superimposed on the duodenal ulcers.

#### SUMMARY

Coexistent duodenal ulcer and gastric malignant lesions are of rare occurrence. In the records of the Mayo Clinic there were only forty-eight proved cases between June, 1911, and January, 1945, inclusive. During this interval, approximately 45,000 patients who had duodenal ulcer and approximately 18,000 patients who had carcinoma of the stomach were seen. Of the patients having duodenal ulcer seen at the Mayo Clinic, 1 in 938 (0.1 per cent) had a coexistent gastric malignant lesion.

The age and sex incidence was about the same as that of carcinoma of the stomach in general.

The symptoms were of long standing in the majority of cases, varying from three days to forty-six years. The average duration of symptoms was 11.3 years.

There did not appear to be any correlation between the levels of gastric acidity and the nature of the peptic lesions. There was wide variation in the levels of gastric acidity encountered.

The roentgenologic diagnosis was accurate in a large percentage of the cases, particularly those in which the examination was made within recent years.

Four of the forty-eight patients in this group had undergone previous surgical treatment of the stomach or duodenum.

It was difficult to evaluate the exact nature of the duodenal ulcers in most of the cases, because in most instances no tissue was removed from the duodenal ulcer for microscopic study. Subacute or perforating duodenal ulcers were described at operation in only four instances. It was assumed that the remaining duodenal ulcers were chronic or healed lesions.

The gastric lesions were predominantly carcinomas. There were one lymphosarcoma and one unclassified high-grade malignant neoplasm. The diagnosis of carcinoma was based on universally accepted histopathologic criteria. Several cases of previously diagnosed carcinoma of the stomach were discarded because it was felt that the histologic changes represented regenerative changes rather than carcinoma.

No explanation could be derived when an effort was made to determine why patients who had duodenal ulcers seldom have malignant lesions of the stomach.

The survival rate in this group of cases was considerably higher than that usually found in cases of carcinoma of the stomach. This was explained by the fact that patients who have duodenal ulcer are "stomach conscious" and are inclined to consult a physician early.

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## THE USE OF STREPTOMYCIN IN SURGICAL PATIENTS

H. A. ZINTFL, M.D., M. WILEY, A. NICHOLS, AND  
J. E. RHODES, M.D., PHILADELPHIA, PA.

(From the Harrison Department of Surgical Research, Schools of Medicine, University of Pennsylvania, and the Department of Surgery of the Hospital of the University of Pennsylvania)

IN THE treatment of infections caused by gram-negative bacteria, streptomycin promises much the same therapeutic effectiveness that penicillin has manifested in the treatment of infections caused by the gram-positive organisms. It remains to be demonstrated whether or not this impression gained from in vitro experiments is confirmed by clinical experience. Although streptomycin is effective in the treatment of certain gram-positive organisms, in general, its effectiveness against these organisms is not as great as that of penicillin. Data, which we wish to summarize, have been obtained by a group of individuals working on several phases of this problem at the University of Pennsylvania.

Streptomycin, first described by Waksman and associates,<sup>2</sup> is obtained from cultures of *Actinomyces griseus*. It is distributed for investigational purposes as a powder varying in color from gray to brown and varying in potency from 200 to 450 units per milligram. A white crystalline material has been prepared which has a potency of 1,000 units per milligram and is now used as a standard of reference but is not available for clinical use. One microgram of this pure material is equivalent to one streptomycin unit. Thus, 10 Gm. is equivalent to 1,000,000 units, a moderate daily dose.

Studies of the acute toxicity of streptomycin indicate that it is definitely more toxic than penicillin, but, nevertheless, the margin of safety between the therapeutic and a definitely toxic dose is wide. Acute toxic symptoms, including palpitation, headache, flushing of the skin, arthralgia, and delayed fever, often occur at dosage levels of 40 to 50 Gm. per day when given in divided doses intramuscularly, and tend to limit the dosage to less than 40 Gm. per day. No evidence of toxicity has been noted following oral administration. Patients have been studied for possible acute toxic effects on the liver, kidney, and cellular constituents of the blood following the intravenous injection of 0.6 Gm. of streptomycin.<sup>1</sup> In six patients, liver function was studied by the bromsulphalein retention, hippuric acid conjugation, quantitative van den Bergh, blood cholesterol, cholesterol-cholesterol ester ratio, prothrombin time, cephalin flocculation, colloidal gold, and thymol turbidity tests before and after the administration of streptomycin. Table I shows that no significant changes in the average values of these tests resulted.

Kidney function as evaluated by per cent of average normal urea clearance, blood urea nitrogen, and blood nonprotein nitrogen showed no significant differences after the administration of streptomycin, as shown in Table II. In addition, routine urinalyses before and every three hours for twenty-four hours after

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TABLE I EFFECT ON LIVER FUNCTION OF THE INTRAVENOUS INJECTION OF 0.6 GM STREPTOMYCIN: AVERAGES OF RESULTS IN SIX PATIENTS

TESTS OF LIVER FUNCTION	BEFORE STREPTOMYCIN	24 HOURS AFTER STREPTOMYCIN
Bromsulfalein (retention in 30 min.)	3.3	1.7
Hippuric acid conjugation (grams excreted)	1.5	1.4
van den Bergh (milligram of bilirubin)	0.3	0.4
Serum cholesterol	142	151
Cholesterol ester (per cent)	60	63
Prothrombin time (per cent of normal)	77.5	81.7
Vegetable flocculation	Neg.	Neg.*
Colloidal gold	Neg.	Neg.*
Turbid turbidity	Neg.	Neg.*

\*Forty-eight hours after streptomycin

The administration of the streptomycin showed no significant changes. The values of the constituents of the blood as tabulated in Table III show essentially no changes in ten patients.

TABLE II EFFECT OF 0.6 GM STREPTOMYCIN ADMINISTERED INTRAVENOUSLY ON RENAL FUNCTION OF SIX PATIENTS

RENAL FUNCTION CRITERIA	AVERAGE BEFORE STREPTOMYCIN	TWENTY-FOUR HOURS AFTER STREPTOMYCIN
Normal urine clearance (per cent of average)	69.1	80.1
Blood urea nitrogen (milligrams per cent)	10.7	9.2
Nonprotein nitrogen (milligrams per cent)	24.3	24.5

Urinolyses every three hours for a period of twenty-four hours after the injection of streptomycin showed no changes.

The only types of chronic toxicity observed clinically have been deafness and vertigo, which have been reported by Hinshaw and Feldman<sup>7</sup> in tuberculous patients who had had large daily doses for several consecutive months. We have noted no evidences of latent toxicity in approximately one hundred patients to whom we have administered the material. In these patients, the largest total dose was 35.0 Gm. over a seven-day period, and the average total dose was approximately 12.5 Gm. over a ten-day period.

TABLE III EFFECT OF THE INTRAVENOUS INJECTION OF 0.6 GM STREPTOMYCIN ON THE BLOOD IN TEN PATIENTS

BLOOD COMPONENTS	AVERAGE BEFORE STREPTOMYCIN	AVERAGE 24 HOURS AFTER STREPTOMYCIN
Hemoglobin (K <sub>2</sub> H photometer)	85.6%	82.2%
White blood cells	6,840	6,990
Neutrophils	71.1%	71.0%
Eosinophils	0.4%	1.2%
Lymphocytes	27.9%	26.4%
Basophils	0.0%	0.0%
Monocytes	1.6%	2.4%

## ABSORPTION, DISTRIBUTION, AND EXCRETION

The absorption, distribution, and excretion of streptomycin in the body depend on the route of administration. When administered orally, approximately 95 per cent was recovered in the feces, and less than 2 per cent was recovered in the urine. Following parenteral administration, an average of 66 per cent of the amount injected was recovered in the urine, and less than 2

per cent was recovered in the feces. There seems to be no indication for intravenous therapy at the present time, since streptomycin is readily absorbed into the blood stream after intramuscular injection.

When streptomycin is injected intramuscularly at the rate of 0.125 Gm. every three hours, it is distributed rapidly to the urine and more slowly to pleural and peritoneal fluids. After administration at this rate for twenty-four hours, streptomycin levels in pleural and peritoneal fluids are roughly equivalent to the levels observed in the blood. In the bile, somewhat lower levels are reached, and in the spinal fluid, little of the antibiotic is found in the absence of meningeal inflammation. The usual body fluid levels obtained following the administration of 10 Gm. per day in eight divided doses intramuscularly are shown in Fig 1. Some of the variations observed are shown by the dotted portions of the graphic representations. It would seem, therefore, from our studies and others, that streptomycin is a drug of relatively low toxicity, not likely to produce late injury except after prolonged administration, and that it is widely distributed in various body fluids other than the spinal fluid after parenteral administration.

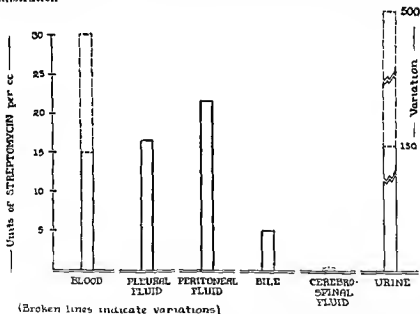


Fig 1—Distribution of streptomycin following the injection of 125,000 units intramuscularly every three hours for twenty-four hours

From the surgical standpoint, we have been interested in four fields of usefulness: urinary tract infections, experimental peritonitis, wound infection, and the prophylactic preparation of patients for operations on the large bowel.

Streptomycin has been used to treat patients whose urinary tract infections have been resistant to penicillin and the sulfonamides. Eighteen of the patients had one or more of the following lesions of the genitourinary tract: prostatic hypertrophy with obstruction, carcinoma, diverticulum, calculus, cystostomy,

nephrostomy, or nephrostomy. The remaining six patients had no anatomical lesions of the genitourinary tract. The entire group of twenty-four patients received 10 Gm. of streptomycin divided into eight intramuscular doses a day for ten days. Fifty-eight per cent of all of the cases were relieved either symptomatically or bacteriologically, 21 per cent had an immediate response but relapsed while still under treatment, and 21 per cent failed to respond.

Two factors may play a part in the relapse of infection in patients who are under streptomycin therapy. First, it is well known that the resistance of certain organisms to streptomycin can change very rapidly, especially when the concentration of streptomycin is relatively low. Second, in severe patients with evidence of severe renal damage, very low urine streptomycin concentrations were found. Fig 2 shows the course in a patient in which both these factors were observed. Urinary concentration of streptomycin in the

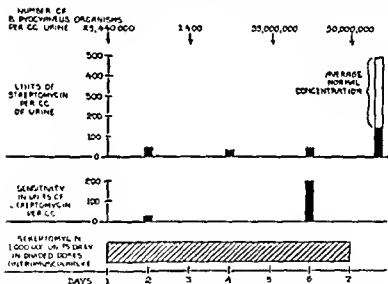
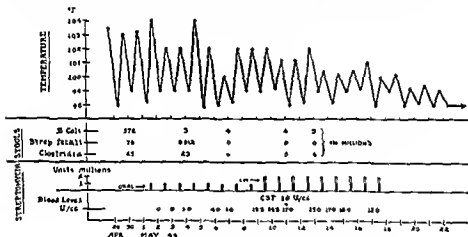


Fig 2—Effect of decreased renal function on streptomycin treatment of *B. pyocyanus* urinary tract infection.

patient varied between 35 and 45 units per cubic centimeter, of urine instead of falling in the expected range of 150 to 500 units. The initial streptomycin sensitivity of the pyocyanus organism was 35 units of streptomycin per cubic centimeter of agar. After receiving 10 Gm. of streptomycin daily for two days, the number of pyocyanus organisms per cubic centimeter of urine fell from 25,000,000 to 1,400. On the fifth day of therapy, the number of organisms per cubic centimeter of urine was 35,000,000. On the sixth day of therapy the sensitivity of the organism was 200 units of streptomycin. It, therefore, seems probable that the very low streptomycin concentration in the urine of this patient was just sufficient to inhibit temporarily the growth of the organisms and at the same time low enough to allow the organism to increase its resistance to streptomycin.

The types of infection were, for the most part, mixed infections of gram-negative and gram-positive organisms. The types of infection and the associated urinary pathologic conditions of the patients were too varied to permit further analysis of this small group of urinary tract infections. The results simply stated are twofold: (1) that 58 per cent of the urinary tract infections which were resistant to several other types of therapy responded to streptomycin, and (2) that the best results were obtained in the patients who had no urinary tract disease apart from the infection. In this small series of urinary tract infections, streptomycin was more effective than penicillin, sulfonamides, or mandelic acid.

The fact that a great many of the patients with associated genitourinary tract lesions had recurrences does not reduce the bacteriologic significance of the results obtained. As long as a primary lesion continues to be present, the patient will be susceptible to recurrent infection. Streptomycin will often, however, produce a remission of the infection and thus prepare the patient for such manipulative or operative procedures as are deemed necessary.





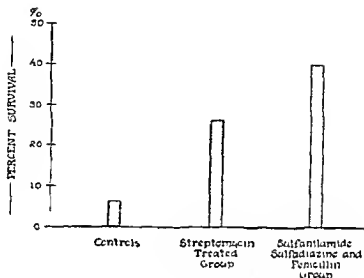


Fig. 4—Animals with peritonitis surviving more than ten days.

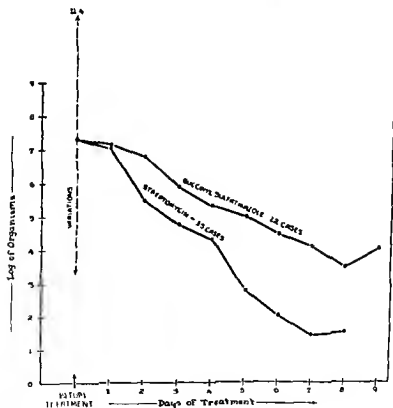


Fig. 5—Effect of streptomycin and succinylsulfathiazole on the number of *B. coli* in the feces.

## PERITONITIS

Theoretically, streptomycin would appear to be the ideal drug for chemotherapy in peritonitis, especially in the common mixed forms arising from the rupture of hollow viscera. The excellence of the results with sulfonamides and penicillin, however, makes one hesitate to change to a new drug without considerable experience with animals.

In a series of experiments recently reported, Murphy and associates<sup>3</sup> obtained seven ten-day survivals among ten dogs in which peritonitis was established by ligation of the appendix and its mesentery, the technique suggested by Bower and modified by Fauley and associates.<sup>4</sup> Three of ten controls survived.

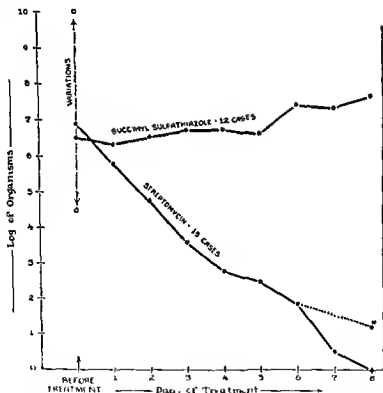


Fig 6—Effect of streptomycin and succinylsulfathiazole on the number of streptococcus fecalis organisms in the feces

In order to get a more definitive infection in subsequent experiments, the Bower technique was modified by opening the appendix after its ligation, as suggested by Meloney and co-workers.<sup>5</sup> Three groups of fifteen animals each in which peritonitis had thus been produced were studied. The first group served as controls and received no special medication. They were allowed water immediately after operation and were allowed to eat on the first postoperative day.

The second group of animals received intramuscularly an amount of streptomycin equivalent to 16,666 micrograms for each kilogram of body weight

every four hours for eight days and then 25,000 micrograms per kilogram every eight hours for two days.

Treatment of the third group of animals was by local sulfanilamide crystals, 0.4 Gm. in the peritoneal cavity at the time of operation followed by parenteral penicillin, 60,000 units of calcium penicillin in a peanut oil-beeswax mixture every twelve hours intramuscularly, and sodium sulfadiazine, 0.65 Gm. intravenously every twelve hours for ten days. Of the control animals, 66 per cent survived the ten-day period, of the streptomycin-treated animals, 26.6 per cent survived, and of the sulfanilamide-penicillin-sulfadiazine group, 40 per cent survived.

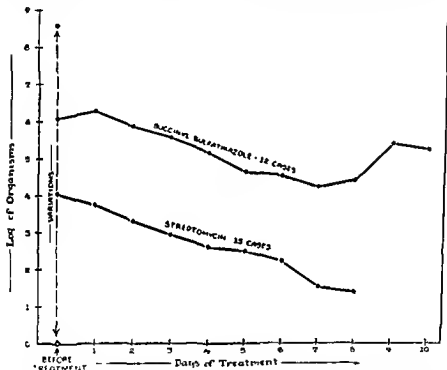


Fig 7—Effect of streptomycin and succinylsulfathiazole on number of clostridial organisms in feces.

On the basis of these experiments, we think one should not substitute streptomycin for the other chemotherapeutic agents in peritonitis until further study provides a sound basis for the change. Further experiments in which streptomycin is used as a supplement to other chemotherapeutic agents are in progress.

#### PROPHYLAXIS IN LARGE BOWEL SURGERY

Several drugs have been advocated in recent years to reduce the flora of the intestinal tract in preparation for surgery. Among these, succinylsulfathiazole is probably the best known. Streptomycin administered by the oral route is especially suitable for this purpose. It is desirable to obtain a more

accurate evaluation, it was administered in doses of 1.0 Gm. per day to fifteen patients for periods of from six to ten days. Quantitative stool cultures were carried out by Miss Marjorie Wiley before treatment was started and at two-day intervals thereafter. By plating out stool suspensions on differential media, counts were obtained for the coliform group of organisms, *Streptococcus fecalis* and Clostridia. The results were compared with similar data obtained by Lockwood and Zintel previously with succinylsulfathiazole. With both drugs, occasional patients show marked deviations from the mean. The logarithms of the counts were plotted against time of drug administration and an average curve was drawn for each drug and each group of organisms. The relative effectiveness of succinylsulfathiazole and streptomycin on *Bacillus coli*, *Str. fecalis*, and the clostridial organisms is shown in Figs. 5, 6, and 7. The figures used are the average of the logarithms, not the logarithm of the averages. Streptomycin, even in the limited dosage employed, was much more effective than was succinylsulfathiazole.

#### SUMMARY AND CONCLUSIONS

Streptomycin is a drug of relatively low toxicity. It is widely distributed in body fluids, except spinal fluid, after parenteral administration, but apparently it does not readily cross the wall of the alimentary tract. Hence it should be given orally if it is to influence the flora of the feces.

It is effective in many urinary tract infections of both gram-negative and gram-positive organisms that have failed to respond to penicillin and a sulfonamide, but not in all. It has, perhaps, a special field of usefulness in infections due to *Bacillus proteus* and *Bacillus pyocyaneus*.

It has exerted a beneficial influence on the course of experimental peritonitis in dogs. The difference was statistically significant when combined with an earlier group of experiments in this laboratory. The therapeutic effect, however, was not as great as that observed with a combination of sulfonamides and penicillin.

Streptomycin appears to be a very effective agent in reducing the bacterial count in the stools. It reduced the coliform organisms to a greater degree than succinylsulfathiazole and reduced the *Str. fecalis* and Clostridia to a much greater extent.

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## 17-KETOSTEROIDS IN THE DIAGNOSIS OF ADRENAL TUMORS

HENRY T. JOHNSON, M.D., AND REED M. NESBIT, M.D.\*  
ANN ARBOR, MICH.

**C**LINICAL syndromes involving masculinizing symptoms have long been recognized, Thomas Cook in 1765 being the first to describe a child with changes probably due to excess androgens. Before 1932 there was great confusion over the etiologic factors involved in these syndromes. Suggested causative agents included adrenal tumors, ovarian tumors, thymic tumors, and other vague endocrine disorders.

Bullock and Sequeira in 1905 published a series of eleven cases of masculinization in women caused by adrenal cortical lesions, and in 1912 Gallati introduced the term "adrenogenital syndrome."

In 1932 Cushing recorded a number of cases of masculinization in which basophil adenomas of the anterior pituitary had been demonstrated. This syndrome is characterized by rapid, plethoric, painful obesity of the trunk and head, acrocyanosis with purplish striae atrophicae, hypertrichosis, osteoporosis, polycythemia, hypertension, insulin-resistant diabetes, and muscular weakness.

Frequently no definite lesion of other endocrine glands is demonstrable, but the adrenals are usually enlarged and may contain small adenomas which Cushing regarded as secondary. That a very similar syndrome may be caused by tumor or hyperplasia of the adrenal cortex also has been definitely established, and in these cases there is an excessive amount of 17-ketosteroids demonstrable in the urine. At present it is thought that both pituitary and adrenal mechanisms may be involved, and there is no general agreement as to which is primary.

With the separation of the Cushing type of syndrome, there remains another clinical type characterized largely by masculinizing changes without the "metabolic" changes also present in Cushing's syndrome. In this so-called adrenogenital syndrome the patients, usually women, show hypertrophy of the clitoris, hirsutism, increase in musculature, deepening of voice, and irregularity or cessation of menses without the other changes of Cushing's syndrome. Etiologic factors have been shown to include ovarian tumors and adrenal cortical neoplasms.

There also appear to be many patients in whom the Cushing syndrome and adrenogenital syndrome are mixed in varying proportions, and it may be postulated that there are many degrees of combinations of "metabolic" factors and androgenic factors. The origin of the defect in many cases of pseudohermaphroditism is not clear, and there are many patients with simple hirsutism in whom no endocrine disorders are demonstrable.

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\*From the Department of Surgery, University of Michigan Medical School.

The differential diagnosis of the etiologic factors in these syndromes on clinical grounds alone is difficult. Roentgenograms of the skull, perirenal air insufflation or pyelograms may be very helpful, and a tumor of the adrenal or ovary at times may be palpable. The recent evidence brought forth by Crooke and Callow<sup>21</sup> that the adrenal cortical tumor group may be differentiated by estimation of the greatly increased urinary androgens in these cases thus becomes of great significance.

The urinary 17-ketosteroids apparently are excretory transformation products of certain adrenal cortical steroid hormones and of testicular steroid hormones, and their output may be considered proportional to the combined secretory activity of these glands. Indirectly they also may give information regarding the anterior pituitary and thyroid glands because of the influence of the pituitary and thyroid hormones upon the adrenals and testes. In most cases, abnormally high rates of excretion are associated with adrenal cortical tumors or hyperplasia and with interstitial cell testicular tumors. Testicular tumor usually can be differentiated by the abnormal size of the involved testis.

The output of 17-ketosteroids in normal individuals has been shown in the Physiology Endocrine Laboratory in this hospital by the method of Robbie and Gilson<sup>22</sup> to be as follows: adult women, 27 to 81 mg per twenty-four hours; adult men, 34 to 150 mg per twenty-four hours. According to Talbot and Butler,<sup>23</sup> children from 4 to 7 years of age excrete an average of 13 mg per day, 7 to 12 years, 40 mg; and 12 to 15 years, 82 mg per day.

Estimation of the total 17-ketosteroids thus may be of great value in differentiating adrenal cortical lesions from pituitary and ovarian and other disorders, but it does not distinguish adrenal cortical hyperplasia from adrenal cortical carcinoma, both of which have excessive androgen production. However, it has been shown that the total 17-ketosteroid output can be separated into alpha and beta fractions, and there is evidence that whereas the alpha ketosteroids are produced by both the adrenals and testes, the beta ketosteroids arise only from the adrenal cortex.

Various workers have shown that normally the beta ketosteroid fraction comprises only about 5 to 15 per cent of the total 17-ketosteroid output, but that in adrenal cortical carcinoma the beta ketosteroid fraction becomes markedly elevated.<sup>2, 23, 24</sup> Thus, the fractionation of the total 17-ketosteroids gives important information which may enable the clinician to differentiate adrenal cortical hyperplasia from adrenal cortical carcinoma. Cushing's syndrome without adrenal tumor is associated with normal or only slightly elevated 17-ketosteroid excretion without increase in the beta fraction.

A survey of the literature reveals less than thirty-five cases of adrenal cortical tumor in which the total 17-ketosteroid output has been determined, and fractionation into alpha and beta portions has been performed in only a very few. We wish to report three proved cases of adrenal cortical carcinoma associated with markedly elevated total 17-ketosteroid excretion in which fractionation into alpha and beta portions has been of definite value in the differential diagnosis.

TABLE I. SUMMARY OF REPORTED HYPERANDROGEN EXCRETION IN PATIENTS WITH PROVED ADRENAL TUMORS

AUTHOR	SEX	AGE	MG. 17 K <sup>2</sup> (TOTAL 17 K <sup>2</sup> )	MG. 17 K <sup>2</sup> (17 K <sup>2</sup> )	MG. 17 K <sup>2</sup> (17 K <sup>2</sup> )	CLINICAL	DISPOSITION	FOLLOW-UP
1 Crooke and Callow <sup>18</sup>	M	25	40 to 64	30		Headache, obesity, plethora, striae, acne, no glycosuria or hypertension, perianal air, left adrenal tumor	Excision of tumor, carcinoma of adrenal cortex	Postop 17 K <sup>2</sup> , 1.9 to 8.3 mg.
2 Crooke and Callow <sup>18</sup>	F	6	124 to 249	120		Swelling of abdomen, pubic hair, large mass in left groin, obesity, acne, hypertension, enlarged clitoris, hypertension, diabetes	Death, autopsy, carcinoma of adrenal cortex	
3 Friedgood and Whiddens <sup>14</sup>	F	-	45					
4 { Friedgood and Whiddens <sup>14</sup>	F	10	325			Microtism, maculose voice, acne, hypertension, polycythemia, acrocyanosis, striae, menstruation at age of 8, enlarged clitoris	Malignant adrenal cortical tumor removed at operation	
5 Talbot et al. <sup>22</sup>	F	13	106	83	83	Large genitalia and pubic hair, acne, increased musculature and size; mass over right kidney, increased osseous development	Excision of tumor, malignant tumor of fetal adrenocortical origin	
6 Fraser et al. <sup>12</sup>	F	50	74			Weakness, hirsutism, baldness, dyspnea, back pain, flared face, acne, blood pressure 170/100, hypoglycemia, decalcification of spine	Autopsy, adrenal carcinoma, 1 kg	
7 Fraser et al. <sup>12</sup>	F	36	109 (total 5 yr.)			Hypertrophic, furunculosis, kidney stones, obesity, decreased stature; head aches, deep voice, amenorrhea, hypoglycemia, decalcification of spine, blood pressure 170/135	Malignant tumor on left, autopsy	
8 Fraser et al. <sup>12</sup>	F	34	132 to 220, 176			Enlarged clitoris, pubic hair, acne, deep voice, body hair, bone age 10 yr.	Operation, encapsulated tumor of fetal adrenal cortical tissue, 110 gm.	
9 Patterson et al. <sup>20</sup>	M	1	24 mg. per liter			Isosexual precocity		
10 Patterson et al. <sup>20</sup>	M	5	27			Isosexual precocity		
11 Patterson et al. <sup>20</sup>	F	Adult	173			Cushing's syndrome		
12 Patterson et al. <sup>20</sup>	F	34	270			Cushing's syndrome		
13 Talbot et al. <sup>22</sup>	F	50	74	51	16	Amenorrhea, abdominal swelling, slight hypertension, x ray, tumor, left kidney; death, pulmonary embolism	Autopsy: tumor of left adrenal, 1,450 gm. carcinoma of adrenal cortex	
14 Anderson et al. <sup>13</sup>	F	25	215					
15 Baumann and Metzgers	F	25	23	23	0	3 wk. P.O. operation for adrenal cortical carcinoma	Recurrent of adrenal cortical carcinoma	

17	Gallow and Crocker?	F	20	25 to 107	Scanty, irregular menstruation, hirsutism preceded (aged and very ill)	Right adrenal cortical adenoma removed, 1939; recurrent petrenal tumor left adrenal tumor	25 to 65 mg., 1939; 168 mg., 1942	Used, death 3 mo. later
18	Gallow and Crocker?	F	41	70 to 74	Virilism, wasting, hirsutism, irregular menstruation	Left adrenal cortical carcinoma		
19	Gallow and Crocker?	F	34	52 to 54	Basophilism with right adrenal cortical carcinoma			
20	Hirschmann?	M	7	273 to 420	Melancholia and manic depression; florid, hirsutism, abdominal swelling	Operation, adrenal cortical carcinoma; P.O. pneumonia		
21	Fingstrom et alio	M	14	24	Hirsutism and weight gain, headaches, palpitation, skin dry, hair falling out	Operation, carcinoma of right adrenal cortex; death soon after operation		
22	Fingstrom et alio	F	14	3.0		Removal of large tumor of adrenal cortex	187 mg. 24 hr. P.O., 77 mg. 10 days P.O.	
23	Fingstrom et alio	F	63	45.0		Operation, removal of carcinoma of adrenal renal cortex	0.9 mg. P.O., clinical recovery	
24	Fingstrom et alio	F	18	54.0		Excision of right adrenal cortical carcinoma	Clinical recovery, 2.8 mg. 10 days P.O.; 2.98 to 6.6 mg. during next 12 mo.	
25	Fingstrom et alio	F	25	171.0		Excision of right adrenal cortical carcinoma		
26	Fingstrom et alio	F	31	170.0				
27	Fingstrom et alio	F	21	210.0				
28	Fingstrom et alio	F	43	537.0				
29	Warrens	F	51	47				
30	Warrens	F	42	600				
31	Warrens	F	49	21.0				
32	Warrens	F	40	12.0	Abdominal swelling, hirsutism, obesity			
33	Johnson and Nesbit	F	2	74.5 21.0	Pubic hair, enlarged clitoris, x ray, right kidney depressed			
34	Johnson and Nesbit	F	31	75	Oligomenorrhea, weight gain, acne, hirsutism, loss of libido, psychomotor, elevated mass above right kidney			
35	Johnson and Nesbit	M	43	81	Previous nephrectomy for left "hyper nephroma"; sections showed adrenal carcinoma, now has large left flank mass and weight loss	X ray therapy	23.4 mg. after x ray; 102 mg. 2 mo. later with metastasis	

\*Probable incomplete twenty-four hour urine specimen determined by method described by Fromm



## CASE REPORTS

**CASE 1**—E. D., a 31-year old married white woman, had a six months' history of loss of libido, scanty menses, fifteen pound weight gain, acne, and hypertrichosis. A vague mass was not easily palpable in the right upper quadrant. There was no hypertension. Pyelograms revealed a faintly calcified mass above the right kidney. Urinalysis was negative. Findings were negative in skull and chest roentgenograms. Basal metabolic rate was -2 per cent. Blood calcium, phosphorus, and alkaline phosphatase were normal. Physical examination, including the genitals, was otherwise negative, 17 ketosteroids: 75 mg. per day (alpha 17 ketosteroids, 19.7 mg.; beta, 55.3 mg.)

On Jan. 13, 1945, the right adrenal gland was explored through a right flank incision, and a well encapsulated, grapefruit sized tumor weighing 600 Gm. was removed. The post-operative course was uneventful without evidence of shock or adrenal insufficiency. Pathologically the tumor was a poorly differentiated adrenal cortical carcinoma with much necrosis. Ten days postoperatively, total 17 ketosteroids excretion was 3.9 mg. per day.



FIG. 1 (Case 1).—Married woman, 31 years of age, before and six months after removal of right adrenal cortical carcinoma. Patient had a six months' history of loss of libido, scanty menses, hirsutism, acne, and weight gain. The operation was followed by complete clinical recovery and normal 17-ketosteroid excretion.

The patient was seen at regular intervals for a period of one year postoperatively, during which time she showed progressive improvement with return of menses, libido, and general well being, and loss of hypertrichosis and acne. Four 17 ketosteroid determinations during this period ranged from 2.94 to 6.6 mg. per day, all within normal limits. There was no evidence of metastasis.

**CASE 2.**—M. S., a 2 year old white girl, was noted at about 1 year of age to have an unusual growth of pigmented pubic hair which gradually increased. She was said always to have had a large clitoris which apparently had not changed during this time. There had been no menstrual flow. Examination revealed a normal child in all other respects. No



FIG. 2.

Fig. 2 (Case 1).—Adrenal cortical carcinoma removed from right adrenal gland. The tumor was solid, well encapsulated, and weighed 660 gm.



FIG. 3.

Fig. 3 (Case 1).—Photomicrograph showing poorly differentiated adrenal cortical carcinoma removed (hematoxylin and eosin, X140)

abdominal tumor was palpable. One urinalysis showed 2+ glycosuria, but all subsequent urinalyses were negative. Blood sugar was 81 mg per cent. Blood pressure was normal. Roentgenograms showed bone age to be within normal limits. Findings from chest and abdominal scout films were negative. Excretory urograms demonstrated the presence of a right adrenal tumor depressing the right kidney; 17 ketosteroids: 74.5 mg per day (alpha 17 ketosteroids, 15.7 mg.; beta, 62.3 mg.). One total 17 ketosteroid determination was 21.0 mg per day, but this lower value was attributed to failure to obtain a complete twenty four hour urine specimen. Estrogens were not measurable.

On April 11, 1945, the right adrenal gland was explored through a right flank incision, and a well encapsulated 6 by 5 cm rounded, solid tumor weighing 72 Gm. was removed. The postoperative course was uneventful without signs of adrenal insufficiency. Pathologically the tumor was an adrenal cortical adenoma undergoing carcinomatous degeneration with numerous hyperchromatic nuclei and neoplastic giant cells. Ten days postoperatively, total 17 ketosteroid excretion was 0.9 mg per day.

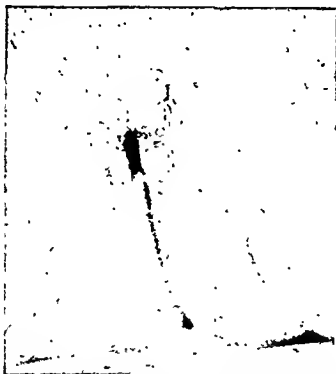


FIG. 1 (Case 2).—White girl, 2 years of age, with excessive pubic hair before removal of right adrenal cortical carcinoma. After operation the child showed clinical improvement and normal 17-ketosteroid excretion, but the pubic hair regressed only moderately.

Six months postoperatively the child showed clinical improvement with increase in well being and normal development. Pubic hair regressed only moderately. There was no evidence of metastasis. Total 17 ketosteroid excretion six months postoperatively remained at 0.9 mg. per day.

CASE 3.—H. W., a 43 year old white man, noted the onset ten months previously of dull pain radiating into the left inguinal region, followed by ease of fatigue, loss of appetite, and loss of weight. A left flank mass became palpable and pyelograms were suggestive of

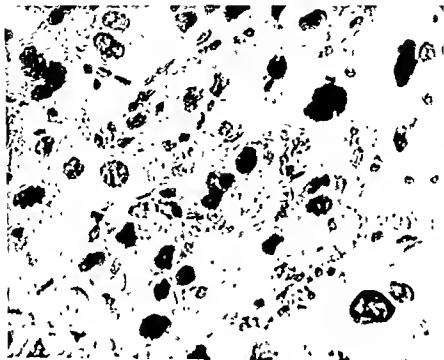


Fig. 6

Fig. 5 (Case 2) — Adrenal cortical adenoma with carcinomatous degeneration removed. The tumor was solid, well encapsulated, and weighed 72 gm.



Fig. 5

## RETROPERITONEAL TERATOMA

### SUCCESSFULLY REMOVED FROM A FIFTEEN-MONTH-OLD NEGRO GIRL

CHARLES M. O'LEARY, M.D., AND BILA HALPERT, M.D., OKLAHOMA CITY, OKLA.  
(From the Department of Surgery and the Department of Pathology, The School of Medicine  
of the University of Oklahoma)

**B**ENIGN retroperitoneal neoplasms with the structure of a teratoma are exceedingly rare, particularly in children. A detailed review of "retroperitoneal mesodermal mixed tumors" in general has just been published by Lahteenmäki.<sup>1</sup> Twenty-three cases of "retroperitoneal teratoid tumors" in infancy and childhood were tabulated by Arnheim.<sup>2</sup> Eighteen of these occurred in children under the age of 2 years. According to Arnheim, his patient, a female infant 3 months old, was the fourth in this age group in whom the tumor was successfully removed. Our patient, a 15-month-old Negro girl, is, presumably, the fifth in whom a large retroperitoneal growth, structurally a teratoma, was surgically removed.

#### REPORT OF CASE

A N. B., a 15 month old Negro girl, was admitted to the University of Oklahoma Hospital, Oct. 15, 1943, with the complaint of progressive enlargement of the abdomen and dyspnea. According to the mother, enlargement of the right side of the abdomen was first noted when the child was 6 months old and for the past three months the entire abdomen had been enlarged. No irregularity of bowel habit was noted. The mother said that the child was small at birth, the exact weight was unknown to her. The child was breast fed for the first six months, during which time she vomited frequently. Eight brothers and sisters were in good health and without known malformations. On admission the child was poorly nourished with the skin dry, loose, and wrinkled; she weighed 26 pounds, 4 ounces. Rectal temperature was 101.0° F.; the pulse rate was 140, the respiration was costal, labored, and 40 per minute. There was marked uniform distention of the abdomen. The presence of fluid could be demonstrated and a large abdominal mass arising apparently from the posterior wall was indistinctly palpable.

Urinalysis was essentially negative. The red blood cell count was 4,500,000, the hemoglobin content was 12.5 Gm.; the white blood cell count was 7,600, with polymorphonuclears 36, and lymphocytes, 64 per cent. Similar results were obtained on Nov. 1, Nov. 15, and Dec. 8, 1943. The Kolmer Wassermann test of the blood was negative. A tuberculin test was negative. Roentgenographic examination of the chest on October 19 revealed marked abdominal distention with elevation of the diaphragm on both sides deforming the cardiac shadow and compressing the right lung. No abnormal tissue shadow was demonstrable. A gastrointestinal series, October 23, disclosed upward displacement of the stomach. At five hours there was gastric residue with barium in the terminal ileum. On October 23, abdominal paracentesis yielded 1,850 c.c. of clear straw colored fluid. Examination for acid fast organisms proved negative. After removal of the fluid, a large indefinitely delineated mass could be felt on the right side of the abdomen apparently fixed to the posterior abdominal wall.

Peritoneoscopic examination on November 4 disclosed no adhesions, no nodules, and no evidence of any inflammatory lesions. The liver, gall bladder, stomach, small intestine, urinary bladder, uterus, Fallopian tubes, and ovaries were visualized and appeared as usual.

Examination with barium enema on November 8 disclosed no intrinsic lesions in the colon but an anterior displacement of the right side of the colon and hepatic flexure by a retro

peritoneal mass. Intravenous pyelograms visualized the calices and pelvis of the left kidney and they appeared normal. A small amount of dye could be seen in the right kidney, obscured by a soft tissue mass. It was surmised that the tumor involved the right kidney.

Röntgen irradiation was given over a fourteen day period (November 15 to 29) using anterior, posterior, and lateral portals with the following factors: 18 ma., 200 kv, distance 50 cm., Thorax filter. A total of 1,200 r. was given to each portal, making the total dose in air 3,600 r. There was no demonstrable effect.

Retrograde pyelograms taken Jan. 4, 1944, revealed the usual configuration of the calices and pelvis of the left kidney. The right kidney was displaced downward and outward with the pelvis elongated, suggestive of extrinsic pressure with slight distortion of the calices. The idea of a neoplasm arising from the right kidney was abandoned.

On January 12 a laparotomy was performed and a retroperitoneal mass, about 22 by 18 by 16 cm, was located. The peritoneal surfaces were smooth and glistening and there were no adhesions. The ascending colon and hepatic flexure were displaced medially as well as the pylorus and duodenum. The mass was adherent to the posterior surface of the liver and distally to the right kidney which was pushed into the iliac fossa. Medially it extended to the hilus of the left kidney. The mass was not adherent to any of the pelvic structures. There were several cystic areas on the anterior surface. From one of these, 40 cc of clear colorless fluid were obtained. In the course of the operation, another cystic area was ruptured on the posterior surface. Removal of the mass was accomplished through a longitudinal incision in the parietal peritoneum, by dissecting away the ileocecal region of the gut and separating the mass from its upper, lower, and dorsal connections. The blood supply originated from the dorsal aspect, apparently from the lumbar arteries, and also from the region of the liver where adhesions were dense. Sulfanilamide crystals (3 Gm) were placed at the site of the tumor and the wound was closed, leaving a soft rubber drain brought out through a subcostal stab wound. The postoperative course was fairly uneventful and the patient was discharged from the hospital February 11, four weeks after the operation. When seen March 22, 1944, she was in good health, and she has been developing normally since.

The specimen removed was an oval, somewhat nodular, fairly well encapsulated mass measuring 15 by 12 by 8 cm. (Fig 1). One surface was smooth, pale gray yellow, and glistening. The opposite surface was ragged and mottled gray yellow and brown. A flap of tissue 11 by 9 cm. and 0.5 to 1 cm thick was attached to one pole and a similar flap 11 by 7 cm to the opposite pole. On the cut surfaces (Fig 2) a capsule 0.1 to 0.3 cm. thick surrounded the mass composed mostly of adipose tissue. Occasional spaces from 0.5 to 3 cm in diameter were filled with soft yellow or transparent jellylike material. Elsewhere, an oval field, 2 by 1.3 cm, of cartilaginous tissue was seen and a triangular area, 1 by 1 cm, of osseous tissue. Microscopically the thin portions of the cyst wall were composed of a broad zone of adipose tissue lobules and a narrow zone of hyalinizing fibrous connective tissue without an epithelial lining. The bulk of the mass was made up of lobules of adipose tissue with delicate or broad septa. The cartilaginous area imitated the structure of hyaline cartilage with the cells unevenly distributed in a homogeneous pink lavender stained ground substance. The cells were single or in small groups within halolike spaces. Perichondrium separated the cartilage from the adipose tissue. The osseous area was bordered, partly by cartilage. Bony lamellae with discernible Haversian systems enclosed marrow spaces containing adipose tissue cells and groups and strands of marrow cells (Fig 3). Within the adipose tissue, separated by a broad zone of collagenous fibers, there were delicate nerve fibrils with round or elongated cell nuclei in a cytoplasm which faded into the fibrils (Fig 4). Within the adipose tissue, elsewhere, there was a cavity lined by a delicate layer of stratified squamous epithelium with three to five rows of cell nuclei and shreds of keratin on the surface. In the corium there were hair follicles and sebaceous glands opened into the hair follicles. There were also some sweat glands (Fig 5). In preparations from the cystic fields, various sized spaces were lined by tall columnar cells with light stained cytoplasm and basally placed nuclei. Infoldings were frequent in some of the lumina. The spaces were separated by broad septa. Other small lumina lined by flat cells connected with the large lumina. Again



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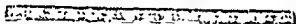


Fig. 1



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Fig. 2.

FIGS. 1 and 2.—The appearance externally and on the cut surfaces of a retroperitoneal teratoma

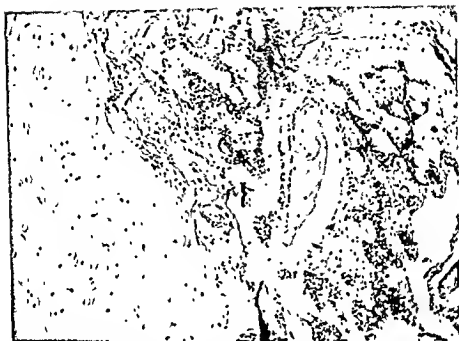


Fig 3.—Microscopic appearance of the osseous area bordered by cartilage. Bony lamellae enclose marrow spaces containing adipose tissue cells and groups and strands of marrow cells (X150)



Fig 4.—Delicate nerve fibrils with round or elongated cell nuclei in a cytoplasm fading into the fibrils (X150)





Fig 5—The lumen of a cavity lined by stratified squamous epithelium with hair follicles, sebaceous glands, and sweat glands in the corium ( $\times 150$ )



Fig 6—Spaces lined by columnar cells with light-stained cytoplasm and basally placed nuclei. One lumen is lined by ciliated columnar epithelium with several rows of reserve cells ( $\times 150$ )

other spaces contained a pink stained amorphous material and the lining cells were flat or absent. One lumen was lined by cuboidal columnar epithelium with several rows of reserve cells (Fig. 6). The line between the epithelium and subjacent connective tissue was usually straight.

#### COMMENT

It seems fairly clear that this teratoma arose from an embryonal anlage within the retroperitoneal space. The growth contained elements of skin and of nervous tissue, hyaline cartilage, osseous tissue with marrow spaces containing red marrow, adipose tissue and lumina lined by tall columnar cells. Judging from the histologic structure, the separation of the anlage must have occurred while the component cells still had the capacity to differentiate into tissues of all three of the germ layers. The benign character of the growth is obvious. Since it possessed, however, the same growth potentialities as the individual, progressive increase of the tissue elements proportionate with the growth of the individual would have occurred. Removal of the growth prevented further interference with the function and development of the adjacent viscera and of the individual as a whole.

#### SUMMARY

The clinical history is presented of a 15-month-old Negro girl with a large retroperitoneal teratoma. The growth was successfully removed and the patient is living and well two years after operation. This is believed to be the fifth recorded case in infancy or childhood in which a retroperitoneal teratoma has been successfully removed.

#### REFERENCES

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2. Arnheim, Ernest E: Retroperitoneal Teratoid Tumors in Infancy and Childhood, *J. Mt. Sinai Hosp.* 10: 333-364, 1943.



Fig 5.—The lumen of a cavity lined by stratified squamous epithelium with hair follicles, sebaceous glands and sweat glands in the corium (X150)



Fig 6.—Spaces lined by columnar cells with light-stained cytoplasm and basally placed nuclei. One lumen is lined by ciliated columnar epithelium with several rows of reserve cells (X150)

Upon the patient's arrival in our hospital, an examination to determine the general condition was carried out, without removal of the dressings unless there was undue pain in the part or an abnormal elevation of pulse and temperature. If an extremity was involved, an effort was made to determine the presence and extent of nerve or blood vessel injury. The dressing was inspected for evidence of hemorrhage and any required roentgenograms were made. If the wounds were anything other than minor, hematocrit and serum protein determinations were made and the patient was typed for transfusion if deemed advisable. Closure was carried out four to six days following débridement if it was at all possible to do so. All elective surgery was made subordinate to the early closure of these wounds. In the operating room, pentathal anesthesia was used in the vast majority of these cases. Following removal of the dressing, the skin surrounding the wound was cleaned with soap and water and ether and irrigated with saline solution. The skin may or may not be painted with an antiseptic. With adequately débrided early wounds of under eight to ten days following débridement little or no granulation tissue has been formed. The skin and subcutaneous tissue overlying the fascia were freed and undermined liberally, if necessary. Frequently, after adequate undermining, wounds which at first appeared impossible of closure come together without undue tension, the skin having retracted and the actual skin loss not being great. Sutures of cotton, silk, or silkworm gut were used with either plain or mattress type sutures, preference being given to plain sutures if the edges did not tend to invert. However, mattress sutures were necessary, in part at least, in the greater number of wounds. In the more severe cases and especially where considerable tension was required, silkworm gut sutures were utilized and we feel that this gave the most satisfactory results in the difficult wounds. Cotton was used in the smaller wounds and the wounds in which there was little or no tension. The sutures were placed closely together at intervals of approximately 1.0 cm. It was frequently felt best, especially in large wounds, to place the sutures before tying them. Postoperative immobilization of the part, we feel, is most important in securing a successful result and plaster casts and posterior splints were used in closures of all wounds of the extremities. We used no sulfonamide drugs locally in any of the wounds. If the patient's hematocrit was below 40, he was given transfusions either before or during the operative procedure. Postoperatively the patient was kept in bed at least until after the first dressing, this being carried out usually on the seventh or eighth day, at which time the greater portion of the sutures were removed. Frequently either altercate or a few central sutures were left in for two or three days longer. The casts, however, were in most instances left off after seven to eight days and early motion was encouraged. Physiotherapy is considered an important aid in early restoration of function. An extremely small number of these patients, unless there was prior evidence of infection, received either sulfonamides or penicillin postoperatively. Small granulating tabs were trimmed with scissors and painted with 10 per cent aqueous solution of mercurochrome. Well-distributed pressure dressings were utilized for the first seven to ten days to obliterate dead space but the pressure was released after the sutures were removed. Drainage was used in thirty-eight cases in this group.

## DELAYED SUTURE OF WAR WOUNDS

MAJOR LOUIS ROSENFELD, MEDICAL CORPS, ARMY OF THE UNITED STATES

**D**ELAYED wound closure was, with the exception of débridement, the operation most frequently performed in military surgery of World War II. Its importance, therefore, in hastening convalescence and expediting the return of the wounded soldier to duty cannot be overemphasized. This report deals with an analysis of 966 wounds, occurring in 315 patients, in which a delayed closure was performed. These patients were treated in a general hospital in Italy from November, 1943, through May, 1945. The cases herein presented include all of the wounds secondarily closed on one general surgical ward in this hospital. In addition to the general surgical type of patient, there were also upon this ward the maxillofacial and plastic cases and a considerable number of chest cases. Very few of the cases in the first two categories required this procedure, the greater portion of the face wounds having been closed in the forward hospitals, whereas, in many of the chest cases, delayed closures were required. In addition to the wounds presented herein, there were numerous wounds in which closure was not feasible and either partial or complete coverage with split-skin grafts was required. Such cases are not included in this analysis. The results in these cases on this one ward are fairly typical of the results obtained in some twelve other surgical wards in this hospital.

The wounds are divided into two groups, those in which primary union was obtained and those in which, following secondary closure, some wound complication resulted. The wounds with complications may be subdivided into the following five groups: (1) cellulitis with purulent exudate, (2) cellulitis without purulent exudate, (3) hematomas, (4) severe stitch abscesses, (5) partial or complete wound separation.

We have been rather stringent in our definition of the last group and considered any wounds to fall into this class in which the wound separation measured 1.0 cm. or greater in length. Of the total number of 966 wounds, 96, or 9.9 per cent, fell into the group of wounds with complications.

### PROCEDURE

The location of our hospital in relation to the actual zone of combat varied over the eighteen-month period and while the hospital remained stationary, the front moved forward. This gave us an opportunity to observe wounds from within a period of twenty-four hours of their receipt up to twenty to thirty days following débridement. At times we had the unique privilege in military surgery of performing both the débridement and subsequent secondary closure. Accordingly the opportunity presented itself for a broader perspective of the problem than had our experience been limited entirely to that of delayed closures. Our experience has led us to the conclusion that the following routine in the handling of the soft tissue wounds results in the most satisfactory closure and the most rapid restoration of function and subsequent return of the patient to duty.

whether or not the time interval, the number of hours elapsing between the occurrence of the wound and the débridement, bore any relation to the success or failure of the subsequent secondary suture. Table IV, of which the facts are demonstrated more graphically in Fig. 1, tends to show that provided an adequate débridement is carried out, the time interval, up to reasonable limits, bears little relation to the success of the subsequent wound closure. This is not indicative that débridement may be delayed with impunity, but merely reveals the relationship in those wounds which were suited to secondary suture. Doubtless delay in débridement in others was responsible for gas-forming infections as well as other types of infections necessitating a much more extensive débridement. These facts are not included and the figures in Table III, therefore, do not give the true over-all picture.

TABLE IV. HOURS TO DÉBRIDEMENT

HOURS	WOUNDS	PRIMARY UNION	PER CENT PRIMARY UNION
1 to 6	158	140	88.6
7 to 12	234	234	92.1
13 to 18	131	122	93.1
19 to 24	140	118	84.2
25 to 36	105	92	87.6
37 to 48	82	79	96.3
49 to 72	79	68	86.0
Over 72	8	8	100.0

Likewise of considerable interest is the relationship of the number of days elapsing between débridement and wound closure to the success of the subsequent closure. This is tabulated in Table V and is likewise shown more graphically in Fig. 2.

TABLE V. DAYS ELAPSING BETWEEN DÉBRIDEMENT AND SECONDARY SUTURE

NUMBER OF DAYS	NUMBER OF WOUNDS	PRIMARY UNION	PER CENT PRIMARY UNION
3	8	6	75.0
4	82	80	97.6
5	148	137	92.6
6	243	236	97.1
7	73	66	90.4
8	61	49	80.3
9	89	77	86.5
10	81	81	96.3
11 to 20	144	118	81.9
Over 20	39	24	61.5

It is of interest to note that closure in six days or less was highly successful in 459 of the wounds closed, with only twenty-two complications and a resultant 95.4 per cent primary union. As the time interval lengthened, the success of closure became less likely. In addition, the difficulty of the procedure was greatly magnified, the older the wound the more granulation tissue present, requiring excision if the closure is to be successful. Frequently wounds which might have been successfully closed at an early date were of necessity covered with a graft when of long duration.

The one prime consideration which we kept constantly in mind in the treatment of these wounds was early mobilization and restoration of function; small granulating areas were not considered an indication for continued immobilization.

# RESULTS

*Wound Complications*—Of the 966 wounds, 96 resulted in some postoperative complication which may be tabulated as shown in Table I. These wound complications will be discussed and further analyzed later.

Considering together the patients returned to either full or limited duty in the Italian Theater, there were 237 such cases, 75.2 per cent of the total (see Tables II and III).

It is difficult to analyze on a statistical basis the reasons for the postoperative complications. There are, however, certain trends which our analysis reveals and which may be pertinent. We have been interested in determining

TABLE I POSTOPERATIVE COMPLICATIONS

	WOUNDS	PER CENT
Cellulitis with purulent exudate	18	1.9
Cellulitis without purulent exudate	13	1.3
Hematomas	6	0.6
Severe stitch abscess	4	0.4
Partial or complete separation (any over 10 cm.)	55	5.8

TABLE II HOSPITALIZATION IN ITALY

DAYS	NUMBER OF CASES	PER CENT
<i>Hospitalization of the 315 Patients</i>		
0 to 30	93	31.1
31 to 60	127	40.3
61 to 90	51	16.1
Over 90	39	12.3
<i>Hospitalization for Those Returned to Full Duty (197 Cases)</i>		
0 to 30	71	36.0
31 to 60	94	47.7
61 to 90	18	9.1
Over 90	14	7.1
<i>Hospitalization for Those Returned to Limited Duty (39 Cases)</i>		
0 to 30	0	0.0
31 to 60	13	33.3
61 to 90	16	41.0
Over 90	10	25.6

TABLE III DISPOSITION OF PATIENTS

DISPOSITION	NUMBER OF CASES	PER CENT
Full duty	197	62.9
Limited duty	39	12.3
To North Africa and other miscellaneous dispositions, ultimate disposition unknown	12	3.8
Zone of interior for soft tissue damage and its complications (nerve and major blood vessel injury excluded) (2 due to thrombophlebitis)	6	1.9
Zone of interior for reasons other than the soft tissue wound	60	19.0

Fortunately, evacuation facilities from the forward installations were excellent. The great majority of patients reached us after a time interval compatible with early secondary suture. The responsibility of carrying out the early closure, therefore, lay primarily on the shoulders of the surgeon in the general hospital.

Another factor, which to a considerable degree is dependent upon the time of closure, but which likewise to some degree is dependent on the judgment of the individual surgeon, is that of whether or not the wound should be excised before closure. In the early wounds, especially those under eight days, previously adequately debrided as mentioned previously, little or no granulation tissue has formed, a considerable portion of the edema has subsided, and the tissues are soft and not fixed. In many of these the skin and subcutaneous tissue can be mobilized and closed. After ten days has elapsed, there is a definite problem due to the firm granulation tissue. The percentage of successful closures of the early wounds which require no excision is high. If the wound is old and excision is of necessity carried out, it is best to perform a total block dissection down to the fascial layer and not temporize with mere trimming of the skin edges and granulation tissue. The results obtained in relation to the necessity of wound excision are tabulated in Table VI and presented graphically in Fig. 3.

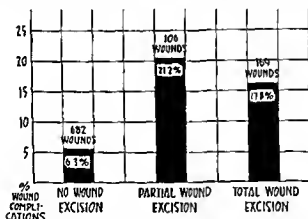


Fig. 3—Per cent of wound complications in relation to necessity of wound excision

We used fine silk or cotton, or silkworm gut suture material, cotton being used for the smaller wounds and those which would close without tension while silkworm gut was used in the most difficult closures, in large wounds, and in those in which considerable tension resulted. In some fifty-nine wounds, a layer closure using buried cotton or catgut was used in order to close fascial defects. This has been utilized especially in the popliteal space and on the fascia lata where closure could be carried out without undue tension. In spite of the 27 per cent complications, we feel that in selected wounds it is of considerable value. The high per cent of successful closures using cotton is not indicative of its being a better suture material, but rather that it was being used on the less difficult wounds. It has been our impression that the instance of stitch abscess formation has been greater when using silk sutures.



TABLE VI PER CENT OF WOUND COMPLICATIONS IN RELATION TO NECESSITY OF WOUND EXCISION

	NUMBER OF WOUNDS	PRIMARY UNION	PER CENT PRIMARY UNION
No excision	652	639	94.7
Partial excision	106	83	78.8
Total	169	139	82.3

TABLE VII. COMPLICATIONS FROM DIFFERENT SUTURE MATERIALS

	WOUNDS	PER CENT OF COMPLICATIONS
Silk	183	10.9
Cotton	434	4.8
Silkworm gut	283	13.7
Layer closure	59	27.0

TABLE VIII. COMPLICATIONS ACCORDING TO SIZE OF WOUNDS

DIAMETER OF WOUND	WOUNDS	COMPLICATIONS	PER CENT OF COMPLICATIONS
Under 2 cm	209	21	10.4
2 to 5 cm	660	60	9.1
Over 5 cm	97	15	15.5

In Table VII are tabulated the number of wounds closed with the respective suture materials and the per cent of complications resulting with each.

The wounds were classified in size according to their greatest diameter and in Table VIII is given the number of wounds in each category with the number and per cent of complications resulting from their closure.

Before closure of the wounds no studies were made to determine the bacterial flora. Clinical judgment alone determined the cleanliness of the wound and its adaptability to secondary suture. Of the total group there were forty-six which were considered dirty wounds. These were treated with either hot wet dressings or excision, or both. In this group twenty-two, or 47.8 per cent, of the patients with dirty wounds had postoperative complications following closure. This emphasized the extreme importance of radical and thorough débridement at the forward installations and the small group of only forty-six wounds is indicative of the excellent débridement done at the evacuation hospitals.

We feel that hot wet dressings should not be used prior to operation on any but the infected wounds. In the first month of work, we treated a few patients with clean wounds with hot wet dressings before surgery and the results were not satisfactory. The leaving of the surgical dressing in situ not only prevents contamination, but the bloody dressings act as an excellent splint. The leaving of the dressing unchanged until the patient is on the operating table assumes that no drains or tight packing have been inserted into the wound at the forward hospitals and in a great majority of cases this was found to have been true.

Of the wounds which did poorly primarily, in the degree of failure was of such severity that a procedure required in

order to secure healing. This was 27 per cent of all the complicated wounds and 2.6 per cent of the entire group. Using the criteria mentioned previously for wound separation, namely, 10 cm. in length, there were many in which the degree of failure was mild, this number being fifty-eight, or 60.4 per cent of the complicated wounds. From the viewpoint which is of primary importance, namely, that of prolonging the convalescence, the analysis reveals that there were twenty-nine wounds in which the failure of the original delayed suture was of such degree that the convalescence was prolonged over that which would have occurred had the original closure been successful. These twenty-nine wounds are equal to 3 per cent of the total and therefore we feel that it is this 3 per cent which might be considered poor results and that 97 per cent of the wound closures terminated satisfactorily. There were no deaths in the series.

### CONCLUSION

These facts substantiate the supposition that following adequate débridement, early secondary suture of the débrided wound is a highly satisfactory procedure. The facility with which wounds can be closed at this early date has been mentioned. It is important that, barring complications, the original dressing not be disturbed until the patient is on the operating table. The importance of immobilization postoperatively cannot be overemphasized and we feel that bed rest the first week is a definite adjunct. We have used practically no sulfonamides postoperatively although practically all of the patients in the group had previously had sulfonamide crystals dusted into their wounds at forward hospitals and many had received either sulfonamides or penicillin, or both, orally and parenterally. The factor of primary importance which we have kept constantly in mind has been that of early mobilization and restoration of function in order to hasten the return of the patient to useful duty in this theater. No attempt will be made to discuss special problems which pertain to wounds in specific localities, such as the face and hands. Needless to say, these two sites withstand closure under tension very poorly. The suture should be small in caliber and we have removed the sutures in the face and neck in from three to five days and in the hand usually on the fifth day without wound disruption. The most difficult sites of closure were the long shoulder and scapular wounds, so frequently and unfortunately longitudinal in direction, often of considerable length, up to 30 to 40 cm., and frequently with considerable loss of substance. Transverse wounds in this locality close much more readily whereas on the extremities, except in the vicinity of the joints, the longitudinal wound lends itself most readily to closure.

The scars resulting from these closures frequently leave much to be desired. With no fascial closure and often sutured under tension, the scars frequently broaden and some have been seen after six- to twelve-month periods that were quite wide. Although muscle hernias obviously are frequently occurring, we have seen only a rare one which was the cause of pain and dysfunction. Doubtless in the years to come, many of these scars will require excision. For the present, however, the method suffices to secure an early closure of the defect with epithelium, early return of function, and a rapid rehabilitation of the patient.

## PLASMA CELL MASTITIS

ELENE A. GASTON, M.D., FRAMINGHAM, MASS.

(From the Surgical Services of the Framingham Union Hospital, Framingham, and the Massachusetts Memorial Hospitals, Boston)

**D**URING the fifteen years since it was first described, plasma cell mastitis has been a subject of increasing interest to surgeons and pathologists. That the disease is one of apparent rarity is attested by the fact that only forty-three cases have been reported in the literature to date. The purpose of this communication is to call this disease to the attention of surgeons again and to report three new cases, two of which present unusual complications.

### HISTORICAL REVIEW

The term plasma cell mastitis was first used by Ewing to describe a benign inflammatory disease of the nonlactating breast. The first published report in which this term was used was presented by Gentile and Cutler<sup>1</sup> in 1931, and was based on cases observed at the Memorial Hospital for Cancer and Allied Diseases, New York, N. Y. Two years later Adair<sup>2</sup> presented detailed reports of the ten cases observed at the same institution up to that time.

Since these preliminary reports,<sup>1,2</sup> five additional contributions have been made in the American literature. In 1931 C. W. Cutler<sup>3</sup> reported a case showing the typical histological characteristics of plasma cell mastitis, with subsequent development of microscopically similar tumors, probably metastatic, in other parts of the body. This important contribution will be considered in some detail. Subsequent contributions to the literature have been made by Rodman and Inglish,<sup>4</sup> Miller,<sup>5</sup> Cramer and Dockerty,<sup>6</sup> Payne, Strauss, and Glasser,<sup>7</sup> and Parsons, Hawthorne, and Clark.<sup>8</sup>

### CLINICAL PICTURE

The importance of plasma cell mastitis lies in the ease with which it may be confused with carcinoma. The disease occurs well within the age limits when carcinoma of the breast may be expected. Adair's patients ranged from 29 to 44 years of age with an average age of 36.3 years, while in the twenty-four cases reported by Cramer and Dockerty, patients averaged 40 years of age. In all published reports the disease has invariably occurred in multiparous women. Elapsed time since the last lactation has averaged four to five years.

Adair has pointed out that the natural history of the disease may be divided into two phases—the acute and the residual. The acute phase consists of a mild inflammatory reaction involving all or a portion of the breast, often associated with increased local heat, redness, and mild tenderness. This phase is transient and the symptoms are usually so mild that the patient does not seek medical advice. After a variable period, ranging from a few weeks to several months, the residual phase, consisting of a nontender tumor, is noted. The tumor at times is accompanied by discharge from the nipple which is

variously described as "watery or creamy" or "puriform." Nipple discharge was noted in twelve of the thirty-four reported cases in which these data were mentioned.<sup>1-4</sup> In none of these cases has a bloody nipple discharge been noted, although in Case 1, to be presented here, such a bloody discharge was present for five months preceding operation.

Examination of the involved breast reveals a firm, nontender tumor mass, with an irregular and often ill-defined border. The mass may occupy any portion of the breast but usually partially underlies the areola. The nipple is retracted and the overlying skin is edematous, giving a typical *peau d'orange* appearance such as is seen in malignant lesions. The axillary lymph nodes are usually enlarged. Signs of local inflammation are entirely lacking.

The physical findings in plasma cell mastitis may so closely resemble those of carcinoma of the breast with attachment to the skin and with axillary metastases that many cases have been reported in which radical mastectomy was done without preliminary microscopic study of biopsy material. The diagnosis may be suspected, clinically, by checking a satisfactory history of the mild acute phase of the disease.

#### DISCUSSION

Since so little is known of the nature, significance, and function of plasma cells, it is not remarkable that the etiology of plasma cell mastitis is still a matter of conjecture. Ewing, commenting on the original cases reported by Adair, concluded that "while bacterial infection is probably a necessary factor in the process, its influence is less prominent than the chemical effect of decomposing fatty material." Following this line of reasoning Rodman and Hughes<sup>5</sup> injected pancreatized milk into the breasts of normal and lactating rabbits as well as into a rabbit in which pseudopregnancy had been induced. A lesion was produced which resembled plasma cell mastitis on microscopic examination. They concluded that "the experiments cannot be held to prove the nature of the substance which is responsible for plasma cell mastitis in the human breast. What they do show, however, is that milk acted upon by enzymes is one way in which the lesion may be produced." The fact that the disease is almost uniformly found in middle-aged, multiparous women who usually give a history of satisfactory lactation suggests that lipids or their breakdown products in some way may be responsible for the unusual cellular reaction. Adair has suggested that improper breast drainage may have an important bearing in this respect.

No satisfactory bacteriologic studies have been reported. Of four cases in Adair's series from which cultures were taken, two showed the presence of unidentified cocci. In two cases material from removed breasts was injected into guinea pigs but the animals did not develop tuberculosis.

Parsons, Heathorne, and Clark<sup>6</sup> observed two cases in which a diffuse comedonastitis coexisted with typical plasma cell mastitis. They speculated that "... if comedonastitis exists prior to the extravasation of material from the ducts it may be responsible for the large quantity of material high in lipid content in the inflammatory area." Focal infection in the form of badly diseased tonsils was advanced as a possible contributing cause in another case.

Payne, Strauss, and Glasser<sup>8</sup> have pointed out the similarity of the basic pathology in mastitis obliterans, a disease described by Ingier in 1909, to that of plasma cell mastitis. The proliferation of the subepithelial connective tissue, the obstruction of the ducts by the latter, and the irregular proliferation of the ductal epithelium are, according to them, the most striking characteristics of both diseases. These authors believe that the massive infiltration with plasma cells seen in plasma cell mastitis is nonspecific and merely indicates a chronic inflammatory reaction of long duration.

#### PATHOLOGY

The gross pathologic lesion of plasma cell mastitis consists of single or multicentric nodules, usually of a yellowish-brown color, occasionally with liquefaction, forming abscesslike cavities. The contents of these cavities, which may be single, multiple, or confluent, vary from puriform material to the color and consistency of butter. The mass varies from soft to firm, often duplicating the consistency of carcinoma. The cut surface reveals thickened and inflamed ducts from which a semipurulent material may be expressed.

On microscopic examination the most striking feature is the massive infiltration of the glandular and interstitial tissues with plasma cells. In some cases these are found in solid sheets, cords, and in round or ovoid masses. More often, however, they are disposed in greatest concentration around the ductal system, and, occasionally, the larger ducts are infiltrated with plasma cells to such an extent that the normal architecture is obliterated.<sup>6</sup> Foreign body giant cells are usually present, sometimes in great numbers, making the differential diagnosis from tuberculosis a matter of concern. These giant cells are often arranged around clear areas which are evidently produced by sheaves of fatty acid crystals which have dissolved during tissue fixation and staining. Eosinophiles in varying numbers are occasionally noted, but other types of leucocytes are usually absent.

A diffuse overgrowth of periductal connective tissue often causes partial obliteration of duct lumen and, by extending into the supporting tissue, accounts for the retraction of skin and nipple which is so commonly noted clinically. Dilated ducts are often filled with cellular debris desquamated from the lining epithelium.

The marked hyperplasia of the epithelium lining the ducts has been commented upon by almost all authors, the cells frequently being piled up eight or ten rows high.<sup>10</sup> That this epithelial hyperplasia presents serious potentialities of malignancy is evident from Case 2, presented here, in which a typical comedocarcinoma coexisted with massive plasma cell infiltration.

Plasma cell mastitis may be indistinguishable from plasma cell tumor of the breast. After a thorough review of the reported cases of extramedullary plasmacytomas, Hellwig<sup>11</sup> concluded that "The plasma cell tumor may arise in almost any situation in the body and may behave clinically as a simple benign growth or as a neoplasm of the most malignant type. From the prognostic standpoint, the localization and the gross appearance seem to be more reliable criteria than the histologic structure." The case reported by C. W. Cutler<sup>4</sup>

demonstrates that such tumors may arise in breast tissue. This patient was a 49-year-old woman from whose left breast a tumor was removed by local excision. Because the microscopic appearance seemed characteristic of plasma cell mastitis, further surgery was abandoned on the basis of a benign lesion. Nine months later a growth with apparently identical microscopic characteristics was found on the right vocal cord, and metastases later occurred in the left sternoclavicular joint, the upper portion of the left breast, and the right antrum.

#### CASE REPORTS

**CASE 1 (Framingham Union Hospital No 57,913)**—A 45 year old white woman, the mother of four children, was admitted to the hospital March 9, 1943. One year previously, following an upper respiratory infection, slight tenderness and heaviness of the left breast was noted. This disappeared spontaneously in about one week. Thereafter she remained well until five months before admission when a slight, bloody discharge was noted from the left nipple. This was intermittent, lasting one day at a time and usually most evident about one week before the onset of the menstrual periods. During the two weeks preceding admission the sanguineous discharge was continuous and, during the last three days, somewhat purulent. A tumor was first noted in the left breast by her physician two weeks before admission. The menstrual periods were regular with no recent change in the type or quantity of flow. There had been no recent change in weight and there was no family history of neoplastic disease.

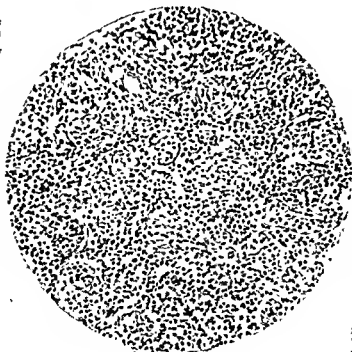
The general physical examination revealed no abnormalities. The right breast was normal in all respects. In the upper, medial quadrant of the left breast was an irregular, nontender tumor 2.5 cm. in diameter. The overlying skin showed a typical *peau d'orange* appearance but there was no attachment to the underlying muscles. Pressure over the tumor caused the discharge of a drop of serosanguineous fluid from one of the nipple openings. Both nipples were slightly inverted but there was, in addition, definite retraction of the left nipple.

Laboratory studies showed the urine to be normal. There was a mild hypochromic anemia with red cell count of 3,700,000 and hemoglobin of 71 per cent. The white cell count was 13,300 with 69 per cent segmented forms, 28 per cent lymphocytes, 2 per cent basophiles, and 1 per cent eosinophiles. Blood Wassermann and Hinton tests were negative. X ray examination of the chest showed no abnormality.

A preoperative diagnosis of intraductal papilloma or papillary carcinoma was made. At operation the mass, overlying skin, nipple, and areola were excised and submitted to the pathologist for immediate section and microscopic study. Following the report of plasma cell mastitis the biopsy wound was closed, the skin reprepared, and a simple mastectomy done through a modified Greenough incision.

Section of the removed mass showed it to consist of two small cavities which were filled with thick, gray brown, purulent material. The cavities were surrounded by an area 4.4 cm. in diameter, orange yellow in color, and rather soft. The remainder of the breast showed no gross abnormalities.

Microscopic examination (Fig 1) showed the tissues surrounding the cavities to be densely infiltrated with plasma cells. Occasional foreign body giant cells and rare eosinophiles were noted. In the peripheral portions of the mass the plasma cell infiltration was less dense and was chiefly confined to the periductal regions. The ducts showed a considerable variation in size with a tendency to retention of secretion and dilatation. The epithelial lining was markedly hyperplastic, in some areas completely filling the lumen. The epithelial cells displayed wide variations in size and shape but no mitotic figures or other evidence of malignant change were noted. There was a moderate increase in periductal fibrous tissue. Sections made from outlying portions of the breast showed less epithelial hyperplasia than was noted within the confines of the tumor, while the periductal plasma cell infiltration was slight or totally absent.



A



B

FIG 1 (Case 1).—A, Low power and B, high power views showing massive plasma cell infiltration and hyperplasia of duct epithelium

The postoperative convalescence was uneventful. When last seen, thirty two months after operation, there was no evidence of recurrence in the scar and no masses were palpable in the opposite breast.

**CASE 2** (Massachusetts Memorial Hospitals No. 297,399) —A 76 year old Negro woman was admitted to the hospital on July 20, 1943, complaining of a tumor in the left breast of two months' duration. There was no history of trauma to the breast, and no local pain or tenderness. The menopause had occurred thirty years previously. She was the mother of ten children, only two of whom were living.

Physical examination showed her to be remarkably well preserved for her years. Except for slight cardiac enlargement with a blowing systolic murmur at the apex and a blood pressure of 240 systolic, and 102 diastolic, the general physical examination showed nothing of note. The right breast was normal. In the upper outer quadrant of the left breast was a firm, nontender, irregular mass 2.5 cm in diameter. This mass was not attached to the overlying skin or to the underlying structures. A few small, discrete nodes were felt deep in the left axilla.

Laboratory studies revealed the presence of diabetes mellitus, with a fasting blood sugar of 340 mg per cent. Red blood cells and hemoglobin were within normal limits. The leucocyte count was 10,000 with 68 per cent segmented forms. X-ray examination of the chest showed no evidence of metastatic disease. The electrocardiogram showed left axis deviation.

Following control of the diabetes, operation was performed July 28, 1943. The mass was biopsied and immediate microscopic examination of frozen section material showed evidence of malignant disease. A radical mastectomy was done, from which the patient made an uneventful recovery. When last examined, Nov. 16, 1945, no evidence of residual malignancy was found.

Section through the tumor revealed it to be lobulated, moderately soft and friable, and to vary from yellow to dark crimson. The regional lymph nodes were firm, enlarged, and, on section, presented a homogenous, moist, grayish pink surface.

Microscopic study (Fig. 2) of sections through different portions of the breast showed a somewhat varied picture. The most striking features were a dense and widespread infiltration with plasma cells associated with an abundant overgrowth of intraductal epithelium which was obviously neoplastic in character. The plasma cell infiltration was most marked in the periductal regions where small numbers of eosinophiles and lymphocytes were also noted. The epithelial cells showed great variation in cytologic structure, low cuboidal, vesicular, pale staining cells prevailing. Frequent atypical mitotic figures were noted. Cells with an identical appearance were seen breaking through the walls of the ducts and infiltrating the surrounding tissue. These infiltrating cells were arranged in thin cords or in irregularly shaped oleoli and were surrounded by, or intimately mixed with, the heavy plasma cell infiltration. No evidence of neoplastic change was noted in the plasma cells *per se*.

Some of the axillary lymph nodes were more or less completely replaced by broad, irregular, medullary cords of epithelial cells similar to those observed in the primary neoplasm. Many atypical nodules were present and there was no attempt at gland formation. Surrounding the epithelial cells were large masses of plasma cells.

**CASE 3** (Newton Hospital No. H-4434) —A 55 year old white married woman was admitted to the hospital June 5, 1942, complaining of a mass in the left breast of two months' duration. Hysterectomy and bilateral salpingo-oophorectomy had been done twenty five years previously. Otherwise past history was noncontributory.

When first noted the mass was about 1.3 cm in diameter but the patient believed there had been subsequent slight enlargement. There had been no nipple discharge and there was no history of local pain or tenderness.

Physical examination showed no significant abnormalities except in the left breast where there was an easily palpable mass 2.0 cm in diameter. The skin overlying the mass had a

\*Dr. E. D. Leonard kindly permitted study and publication of this case.



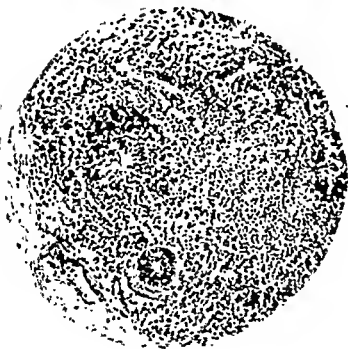


Fig 2 (Case 2) —A, Low power view showing massive plasma cell infiltration surrounding ducts, one of which shows malignant change B, In-

B

tra ductal epithelium showing closely packed, anaplastic cells.

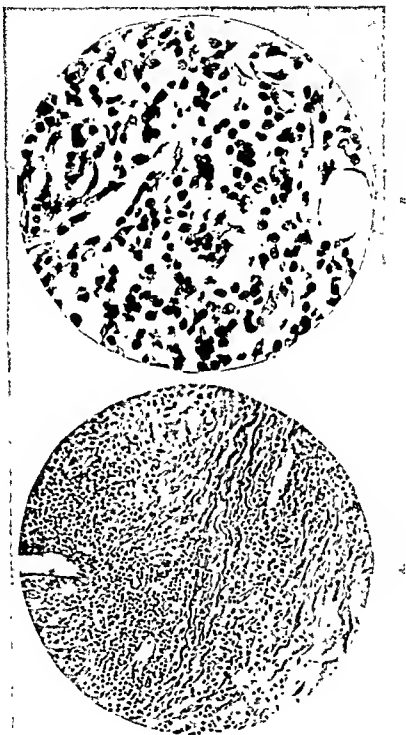


Fig 3 (Case 3) —A. Low power view showing increased fibrous tissue atroma diffuse plasma cell infiltration with periductal concentration and paucity of ducts B. high power

typical peas of orange appearance but there was no retraction of the nipple. No nodes were palpable in the axilla and laboratory studies showed no significant deviation from the normal.

At operation the tumor and overlying skin were excised with a wide margin. Microscopic examination of frozen section material was mistakenly interpreted as showing evidence of malignancy and radical mastectomy was performed. The postoperative recovery was uneventful and the patient has remained well.

Section of the removed tumor showed it to consist of a stony hard, white mass 2 cm. in diameter with no evidence of encapsulation or central softening. Serial section of the remainder of the breast showed nothing of note. Seven lymph nodes were found in the axillary fat, ranging from 0.5 to 1.0 cm. in diameter.

Microscopic examination of the tumor (Fig. 3) showed an increase of fibrous tissue stroma, diffusely infiltrated with plasma cells, but with a notable periductal concentration. At scattered points foreign body giant cells were seen singly or in small groups. A few clear areas, probably produced by dissolved sheaves of fatty acid crystals, were surrounded by giant cells. The ducts, which were small and relatively few in number, showed definite hyperplasia of the lining epithelium. No abnormal proliferation, invasion, or other evidence of malignancy was noted. Appropriately stained sections showed no tubercle bacilli. The axillary nodes showed no histopathology.

#### DISCUSSION

The uniformity of the clinical and microscopic findings in typical plasma cell mastitis, such as in Cases 1 and 3 reported here, is striking. At the same time doubt has been expressed as to whether the plasma cell reaction is a primary and essential part of a clinical and pathologic disease entity.<sup>6</sup>

From the clinical standpoint it would seem that such symptoms as tumor, nipple discharge, and skin and nipple retraction could be satisfactorily explained on the basis of epithelial hyperplasia and periductal fibrosis. Perhaps the only part of the clinical picture which might be attributed to the plasma cell reaction is the early acute phase described by Adair.

From the histologic standpoint it is well known that plasma cells are found in a great variety of disease processes in which they are considered important only as indicating the presence of an inflammatory process of long duration. Therefore, if the plasma cell reaction is merely incidental to some other pathologic process, the advisability of the term plasma cell mastitis, which places stress on this secondary manifestation, has been questioned. To overcome this nomenclatural disadvantage the suggestion has been made<sup>12</sup> that plasma cell reaction be used as a suffix to point out this unusual tissue response, at the same time naming the pathologic condition which may have elicited it. Thus, Cases 1 and 3 might be termed "glandular cystic hyperplasia with plasma cell reaction" or "chronic mastitis with plasma cell reaction," while Case 2 could properly be termed "comedocarcinoma with plasma cell reaction."

In Case 1 there was a sanguineous nipple discharge. In view of the marked hyperplasia of the epithelium lining the ducts, it seems probable that this symptom will be encountered in a small percentage of cases.

Case 2 is of particular importance because it illustrates the concomitant development of comedocarcinoma in a breast which was the site of a plasma cell reaction. While this is the first case that has come to our attention in which the two conditions have coexisted, the epithelial hyperplasia noted by all authors suggests that such a combination is more than coincidence. This case, together with that reported by C. W. Cutler in which the disease, or one

microscopically identical with it, metastasized as a plasmacytoma, suggests that plasma cell mastitis, while usually a benign disease, has definite malignant potentialities which may develop in either, or possibly both, of two directions. (1) As a malignant epithelial neoplasm of the comedocarcinoma type, probably the result of dedifferentiation of the hyperplastic ductal epithelium or (2) as a malignant plasmacytoma. In addition, Parsons, Henthorne, and Clark observed two cases in which local recurrence, without distant metastases, followed simple excision of the tumor mass.

These considerations would seem to clarify the problem of treatment. Biopsy and immediate microscopic examination of frozen section material should be carried out in all breast tumors, including those in which the clinical findings are characteristic of malignancy. When the diagnosis of plasma cell mastitis is established histologically, simple mastectomy would seem to be the operation of choice, at least until more is known of the etiology and natural history of the disease. Sections from many parts of the removed breast should then be carefully studied for evidence of malignancy. If such evidence is found, subsequent removal of the pectoral muscles and radical axillary dissection are, of course, indicated. Even though histologic evidence of malignancy is not found, careful follow-up examinations for evidence of local or distant recurrence should be made for several years following operation.

## SUMMARY

- 1 The etiology and pathology of plasma cell mastitis are reviewed
- 2 Three new cases of plasma cell mastitis are reported. One of these patients had a sanguineous nipple discharge for five months preceding operation. In another there was a coexistent comedocarcinoma which had metastasized to the axillary nodes.
3. The relationship of plasma cell mastitis to malignancy is discussed
4. The treatment of choice consists of simple mastectomy, followed by careful histologic study for evidence of malignancy
- 5 The importance of adequate follow-up study is stressed.

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## SECONDARY DAMAGE IN WOUNDING DUE TO PRESSURE CHANGES ACCOMPANYING THE PASSAGE OF HIGH VELOCITY MISSILES

E. NEWTON HARVEY, PH D., I. M. KORS, PH D., G. OSTER, PH D., AND  
J. H. McMILLIN, PH D., PRINCETON, N. J.

(From the Biological Laboratories, Princeton University)

### INTRODUCTION

BY PRIMARY damage in wounding we refer to injury directly traceable to changes accompanying the movement of the missile. When a high-velocity bullet enters the body and plunges through tissue, it is obvious that material in its path will be thoroughly disintegrated. A *permanent cavity*, filled with blood and pulped cells, is gouged out. In addition, immediately behind the moving missile, a large *temporary cavity* appears, many times the cross-sectional area of the missile itself. This temporary cavity quickly subsides, but tissue at its periphery has been greatly stretched and cells may be injured. Small blood vessels and capillaries are ruptured. There is left a considerable *region of extravasated blood* around the missile track. Changes in these three regions—the temporary cavity, the permanent cavity, and the region of extravasated blood—result in primary damage, which might be used as a direct measure of wounding. Photographs illustrating these phenomena will be found in a previous paper<sup>1</sup> which contains references to the literature.

We propose in this communication to consider what may be called secondary damage in wounding, which is the result of pressure changes accompanying the passage of a bullet. Reference has already been made (Puckett and associates<sup>2</sup>) to such effects in the abdomen where perforation of the intestines was found to be connected with rapid expansion of gas pockets, which stretched and tore the tissues, acting like secondary cavities. Secondary damage in wounding is quite comparable to injury from underwater blast where pressure changes cause damage to men and animals in the water. This damage also occurs only at air pockets in the body, resulting in intestinal perforations or lung hemorrhage (see Williams,<sup>3</sup> McMullin and co-workers,<sup>4</sup> Corey,<sup>5</sup> Friedell and Ecklund,<sup>6</sup> Clark and Ward,<sup>7</sup> and Clark<sup>8</sup>).

### MEASUREMENT OF PRESSURE CHANGE

The pressures dealt with in this study have come from  $\frac{1}{8}$  or  $\frac{3}{16}$  inch steel spheres, weighing 130 and 440 mg., respectively, which have struck the liquid or tissue with velocities varying between 2,800 and 4,800 feet per second. The magnitude of the pressure change is great and the duration must be measured in microseconds or milliseconds. Nevertheless, several methods of measurement are available.

An exact method, which follows rapid time changes in temperature, measured in microseconds, makes use of a piezoelectric crystal tourmaline. When

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subjected to hydrostatic pressure, tourmaline develops a charge the voltage of which can be amplified and recorded with a cathode ray oscillograph. Such records have recently been made in the Princeton biology laboratories when a high velocity steel sphere is shot into a tank of water or passes through the abdomen of an anesthetized cat (Harvey and associates<sup>11</sup>).

Other types of pressure gauge are too slow to follow faithfully the rapid pressure changes but will indicate the direction of pressure change. A simple and instructive method is the use of small masses of gas as pressure indicators. For this purpose rubber balloons about  $\frac{1}{2}$  inch in diameter are suspended by threads attached to the bottom of a tank of water with plexiglass sides. Steel spheres are shot into the water among the balloons and a high speed moving picture of the changes is taken. Contraction of the balloons indicates increased pressure, and expansion decreased pressure. Four disadvantages may be noted, (1) the balloons may not instantly respond to pressure changes, (2) once the balloons have been compressed in a pressure increase they expand and pulsate with their own period superposed on slower pressure changes in the tank itself, (3) shape changes also accompany volume changes of the balloons, so that increase or decrease in volume cannot be determined accurately, (4) introduction of the balloons so changes the system that pressure distribution in absence of balloons cannot be recorded accurately. These four disadvantages combine to prevent an accurate measure of pressure changes from balloon size and Boyle's law, but the trend in pressure is definitely apparent. Their great advantage lies in the fact that pressure changes in many different locations can be visualized simultaneously. The balloons also imitate very closely the behavior of gas pockets in the animal.

#### THE SIMILARITY OF A SHOT INTO WATER ON FLESH AND AN UNDERWATER EXPLOSION

Practically all observers of wounding by high velocity missiles have compared their effects to an explosion in the body because of great damage to tissues at some distance from the bullet path. In any underwater explosion there is formed a large cavity or "bubble" quite comparable to the temporary cavity left by a high velocity missile. The cavity behind a shot is shown in Fig. 1 and the explosion in Fig. 2. After attaining a maximum size, these cavities contract and then pulsate at a rate which is dependent on their maximum volume. The maximum volume in one case (the shot) is proportional to the kinetic energy of the striking missile, in the other case (the explosion) to the heat of detonation. It is therefore possible, knowing the striking energy of a missile, to calculate not only the size of the temporary cavity it will produce, but also to state that the effect will be the equivalent of a definite number of milligrams of TNT exploded in the body.

In both cases very similar pressure changes occur around the cavity. We shall first compare the pressure changes in an underwater explosion with those which accompany a shot into water in a tank and then apply these to conditions in the body. The use of water is justified since the soft tissues behave like a liquid system. The pressure changes are of three kinds: (1) shock wave pres-

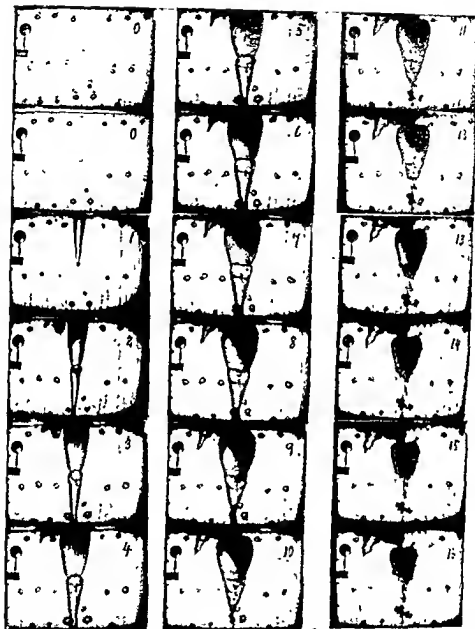


Fig 1—Motion picture (166) frames (2160 per second) of a  $\frac{1}{8}$  inch steel sphere (Impact velocity 3,000 feet per second) striking the surface of water (indicated by arrow) in which are suspended small rubber balloons. The development of the temporary cavity is well shown. Pressure changes in the water are indicated by contraction and expansion of the balloons. Successive frames are numbered. The vertical dots on the left are 5 cm. apart.

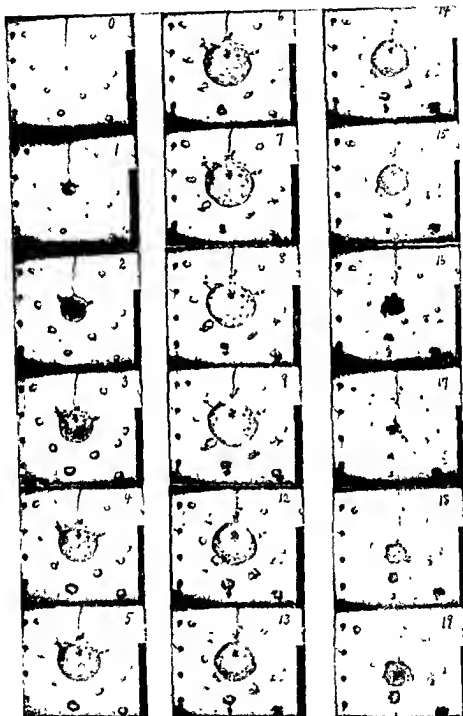


Fig 2—Motion picture (25 D) frames (about 2160 per second) of the detonation of a cap containing 30 mg of explosive. The expansion and first contraction (frame 17) of the explosion bubble are well shown. Small rubber balloons have been suspended in the water to detect pressure changes. The vertical row of dots on left are 5 cm apart.



tures or sharp, high-pressure pulses, formed when the missile hits the surface of the water or when the defonation occurs, (2) very high-pressure regions in front of the moving missile or around the early detonation bubble; (3) relatively slow, low pressure changes accompanying the expansion and contraction of the temporary cavity formed behind the missile or around the expanded bubble of gas from the explosion of the underwater charge. Considerable space must be devoted to these pressure changes in simple liquid systems in order to understand what happens in tissues.

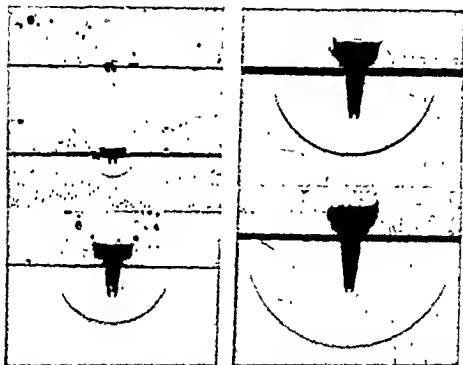


Fig 3—A series of spark shadowgrams (S59, S31, S71, S90, S21) of  $\frac{1}{8}$  inch steel spheres taken at successively longer time intervals after the sphere has hit the water surface. Note how the shock wave, moving 4300 feet per second, leaves the retarded sphere behind. The striking velocity in all shadowgrams is 3000 feet per second except the second where it is 1,772 feet per second.

#### SHOCK WAVES IN LIQUIDS

An exhaustive study of shock waves formed by small high-velocity missiles striking water has been made in this Laboratory by McMillen<sup>9</sup> and McMillen and Harvey<sup>10</sup>. These sharp high pressure pulses move away from their point of origin with the velocity of sound, 4,800 feet per second<sup>11</sup>. The shock wave front pressure rises instantly to a high peak value and falls off more slowly behind. The peak pressure varies directly as the projected cross sectional area of the missile and as the square of its impact velocity, but inversely as the

<sup>11</sup>A shock wave in water moves slightly more rapidly than a sound wave, but the increase is not great, about 5.5 per cent for a shock wave of 14,500 pounds per inch<sup>2</sup> peak pressure.

distance from point of origin. At the water surface the shock wave pressure becomes enormous and equals the pressure on the face of the striking sphere. Energy for shock wave formation thus comes from the kinetic energy of the missile. It is obvious that tissue struck by such high-pressure pulses might be damaged. The evidence for and against such damage will be considered shortly.

Shock waves from underwater explosions are similar to those from missiles hitting water. Waves from large detonations may be measured in tons per inch<sup>2</sup> and are known to injure or to kill men at a considerable distance in the water. The energy for their formation comes from the heat of explosion, about one-third to one-half of which goes to form the shock wave, the remainder going into the expansion of the gas bubble.

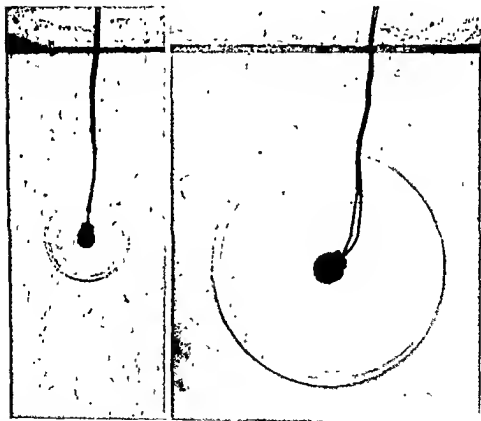


Fig. 4—Spark shadowgrams of the shock waves from a detonator cap containing 30 mg of explosive

Because of the high pressures in a shock wave, the water is compressed and the refractive index changes. This change is shown clearly in a spark shadowgram. In Fig. 3 is reproduced a series of shock waves moving away from a steel sphere striking the surface of the water, and in Fig. 4 shock waves from an underwater explosion. In both cases the spherical wave appears as an advancing

absence-of light band (dark in a print) changing to a light band behind the wave front. The small secondary waves are due to vibration of the steel sphere. Similar waves move through tissue when struck by high-velocity missiles.

#### MOVING SPHERE PRESSURE

The pressure immediately in front of a moving sphere is enormous, measured in thousands of atmospheres. It is numerically equal to  $\frac{1}{2} \rho V^2 C_D$ , where  $\rho$  is density of the medium,  $V$  velocity of the missile, and  $C_D$  the drag coefficient, which, for spheres in water, has the value 0.298. This moving sphere pressure is visualized in Fig. 5, a spark photograph of a steel sphere moving in water behind a grid of lines on a plexiglass plate. The distortion of the lines in front and also at the sides of the sphere is due to a change of refractive index resulting from compression of the water. The moving sphere has its analogy in an underwater explosion, where it is represented by the enormous pressures of the hot gases formed during the detonation.

The moving sphere pressure falls off in front of the sphere to values above an atmosphere, then the pressure rises again, to culminate in the shock wave peak. Since the shock wave is spherical around an explosion, the pressure distribution is radially symmetrical with the detonation point as a center, whereas the missile starts a hemispherical wave from the water surface and pressure gradients are axially symmetrical around the bullet path; a high pressure always exists in front and at right angles to the missile as it advances.

#### PRESSURES AROUND THE EXPLOSION OR TEMPORARY CAVITY

When the shock wave has moved well away from its point of origin and the temporary cavity or explosion bubble is still expanding, the pressure distribution becomes greatly changed. Subatmospheric pressures follow the previously described increased pressures and extend over wide regions around the cavity. They change as the temporary cavity or bubble pulsates, increased pressure accompanying expansion and decreased pressure accompanying contraction. Since these relatively slow, relatively small pressure changes are of great importance in wounding, they have been measured accurately and will be considered in detail.

Making use of small air-filled balloons as pressure indicators, a general idea of the pressure changes in a tank of water can be obtained from Figs. 1 and 2 which are prints from individual frames of a high-speed moving picture (about 2,000 frames per second). In Fig. 1 the balloons reveal the pressure distribution during a high-velocity shot into water and in Fig. 2 after a detonation under water.

In both figures the zero frame shows the size of balloons before the shot. In Frame 1, balloons near the initially expanding cavity are small, indicating high pressure due to the shock wave. In Frame 2 balloons near the still expanding cavity are large, while those away from the cavity are small. The pressure region has moved out as the cavity expands and is followed by a region of subatmospheric pressure around the cavity. This subatmospheric region increases in size, and in Frame 3 practically all the balloons in the tank are

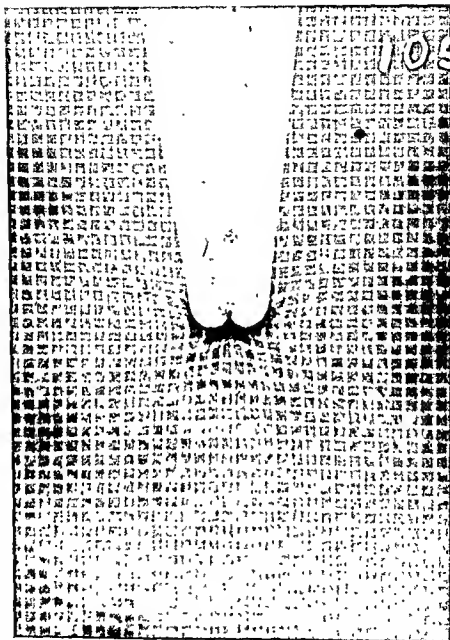


Fig. 5—An enlargement of a spark shadowgram (D103) of the region around a  $\frac{5}{16}$  inch steel sphere (impact velocity 2,000 feet per second) which has penetrated 5 cm. of water. The high pressure near the missile is revealed by the distortion of a 1 mm grid placed between the spark and sphere.

much larger than in Frame 0. In later frames the balloons undergo shape changes and volume oscillations while the cavity (or bubble) is still increasing in volume. These minor oscillations are believed to indicate the natural period of the balloons, about 0.002 second.

There appears to be a relatively long period of subatmospheric pressure following the initial sharp pressure increase of the shock wave and while the cavity is still expanding. This decreased pressure is due in part to overexpansion of the cavity (or bubble) and in part to Bernoulli lowering of pressure as a result of the high radial velocity of water around the expanding cavity.

A very considerable difference exists in the initial pressure within the cavity behind a bullet and within the bubble of an underwater explosion. In the former the pressure is always subatmospheric from the start. The missile pushes the water aside as it moves forward, compressing and imparting momentum to the liquid, thereby leaving a partial vacuum, because not enough air flows in to maintain atmospheric pressure. In an explosion cavity or bubble, made up of the gaseous products of explosion, the pressure is at first positive and very high. It is this gas under pressure formed in a few microseconds that suddenly compresses the water, starting the shock wave and giving the water its momentum.

In either case, once momentum has been imparted to the water, its inertia leads to an overexpansion of the cavity, with the development of subatmospheric pressures in the liquid. When this inertia is overcome by the tank walls and pressure of the atmosphere, the cavity volume decreases, resulting in contraction to a minimum volume and a second development of pressure. The air in the cavity is compressed. Following this there is a second expansion. The cavity then pulsates at a rate which can be calculated from the energy delivered to the water. Alternate increase and decrease of pressure accompany the pulsations.

The second pressure development can be seen clearly in Frame 17, Fig. 2. All the balloons around the contracted mass of explosive gases are greatly contracted. The second pressure development during the cavity minimum in the shot into water (Frame 16, Fig. 1) is not so marked but can be recognized. The amplitude of pulsations of the temporary cavity are also not as great.

The pressure changes during cavity pulsation are best seen in a pressure record. Such a tourmaline crystal record, of the first three pulsations after a shot ( $\frac{3}{16}$  inch sphere moving 3000 feet per second) into a tank of water, is shown in Fig. 6. The time scale is in milliseconds and the shock wave peak is a thin vertical line that extends off the record. The small rapid pressure changes with a frequency of about 3,000 per second, superposed on the first part of the record, probably come from the vibration of the tank walls. It was possible to produce similar vibratory pressure changes by striking the tank with a hammer.

In Fig. 7 are reproduced frames from a motion picture of the events in the tank, taken at the same time as the tourmaline crystal pressure record. By comparison of picture frames and crystal record it is possible to correlate movement and pressure. It will be observed that when the temporary cavity volume is at a minimum the pressure is approximately a maximum. The first peak

comes 11 milliseconds after the shock wave and represents a pressure of about 60 pounds per inch<sup>2</sup>; the second peak is 10 milliseconds later, 21 pounds per inch<sup>2</sup>; the third 9 milliseconds after the second, about 7 pounds per inch<sup>2</sup>.

Subatmospheric pressures between the peaks are particularly marked. The first two, about 15 pounds per inch<sup>2</sup> below the atmosphere, may even indicate a slight negative pressure, that is, a pressure below zero or a tension.

It should be particularly noted that the record shows no pressure changes which occur with the same frequencies as the small oscillations of the balloons of Fig. 1. This fact indicates that these balloons must be oscillating with their own natural frequency, about 500 per second, which is superimposed on the larger volume changes connected with cavity behavior.

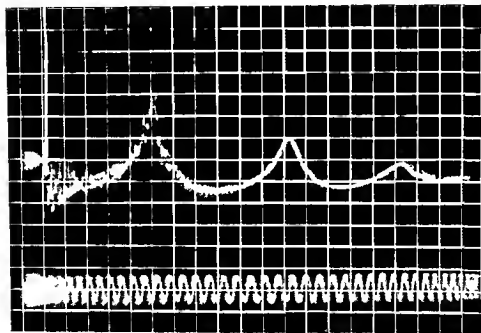


Fig. 6—A record of pressure changes in the tank of water during the shot reproduced in motion pictures of Fig. 7. The first peak at the left is that of the shock wave pressure. The first, second, and third peaks, corresponding to three minimum cavity volumes, are well marked. Note the subatmospheric pressures below the base line. The high frequency (3 000 per second) pressure excursions in the first third of the record are due to vibration of the steel frame of the tank. One vertical division represents 131 pounds per inch<sup>2</sup> pressure. The time record is 1000 cycles.

In the human body somewhat similar changes must occur during the passage of a bullet, an increased pressure followed by a decreased pressure. However, mass of material and elastic walls may be expected to modify the movements and the pressures developed. After a shot through the abdomen of a cat, the expansion of cavity to maximum volume occupies much less time than in a large tank of water (see Harvey and associates<sup>11</sup>). The important difference between the water and the abdomen shot lies in cavity behavior after collapse. Microsecond roentgenograms of the cat's abdomen show no second expansion of the

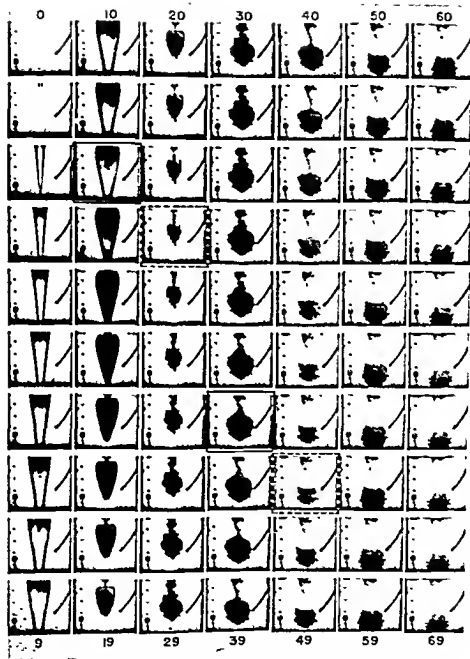


Fig. 7.—Frames from a high-speed (2,126 frames per second) motion picture of a  $\frac{3}{16}$  inch steel sphere entering a tank of water with a velocity of 3,600 feet per second. The dots to the left are 5 cm. apart. The crystal gauge is visible as the slightly curved line at right. The crystal pressure record is reproduced in Fig. 6 (Ex. 3 of Jan. 18, 1946).

temporary cavity. Because of the small entrance and exit holes in the abdominal wall, air cannot rush into the cavity as in a water shot. The cavity space is filled almost entirely with water vapor and practically complete collapse takes place. The slight oscillations in pressure which occur can be attributed to gas pockets already present in the intestines.

#### POSSIBLE DAMAGE FROM SHOCK WAVES IN GAS-FREE TISSUE

Possible damage from shock waves will presumably depend on their intensity. The question that concerns us is whether or not the waves generated by small high-velocity missiles are destructive outside the limits of the observed stretching and tearing caused by the temporary cavity. It might be predicted that a mass of tissue suddenly struck by a pressure pulse of 10 to 60 atmospheres, traveling, 4,800 feet per second, would be seriously affected. However, it is well known that hydrostatic pressure itself, even when applied for considerable time periods, does not affect tissues unless the pressure is excessive, greater than 500 atmospheres (see Cattell<sup>13</sup> and Brown<sup>14</sup>). Since shock waves last a very short time and involve only slight displacement of the medium, it is possible that liquid tissue could withstand the slight displacement without damage.

One experiment may be cited to show that even such delicate cells as human red blood corpuscles are not damaged when struck by shock waves. A dilute suspension of corpuscles in Ringer-Locke solution was placed in a steel cylinder,  $8\frac{1}{16}$  inches internal diameter, filling it to a depth of 9 inches. A  $\frac{1}{4}$  inch steel sphere was then shot into the water with a velocity of 3000 feet per second. Every corpuscle in the cylinder must have been exposed to the high pressure shock waves generated by the sphere. In addition, many corpuscles were subjected to the agitation and movement accompanying the cavity formation, which blew one-half the blood suspension out of the cylinder. Nevertheless, there was less than 1 per cent hemolysis in the remaining blood, no more than is frequently observed on shaking blood with air.

A further test of shock wave effects on tissues was made by tying frog hearts in various positions in a tank of Ringer's solution and then shooting a steel sphere among the hearts. A high-speed moving picture was taken and the hearts were examined carefully after the shots to determine any change in amplitude or rate of heart beat. The peak pressure pulse that struck each heart could be calculated from the impact velocity and projected cross-sectional area of the sphere and the distance and angle of the heart from point of impact of the missile on the water surface.

In Fig. 8 are reproduced frames from such a high-speed moving picture of a  $\frac{1}{8}$  inch steel sphere striking the water with a velocity of 3,100 feet per second and an impact energy of 6 times  $10^6$  ergs. The hearts, tied to vertical strings in Ringer's solution, were beating well before the shot. From the moving picture the exact position of the cavity at all phases of expansion and contraction can be seen.

Some of the hearts ( $C_1$ ,  $C_2$ ,  $C_3$ ) were engulfed by the cavity and either torn loose or damaged so that the beat ceased or greatly slowed. Others ( $B_1$ ,  $B_2$ ,  $B_3$ ) were outside the range of the temporary cavity. Two of these hearts ( $B_1$  and



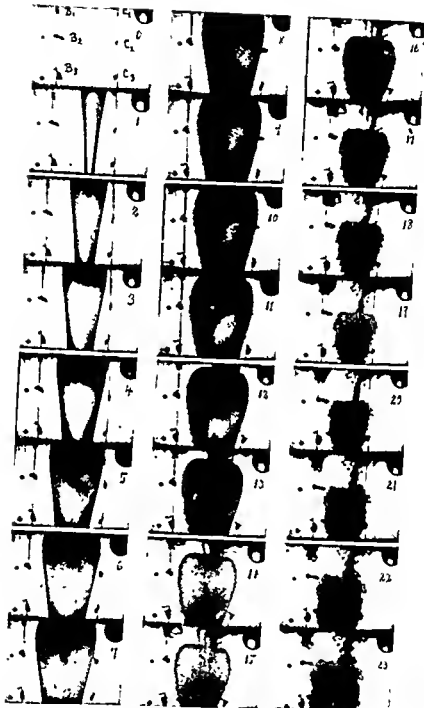


Fig. 8.—Frames (2400 per second) from a motion picture (145) of six frog hearts tied to two vertical strings in a tank of Ringer's solution. The surface of the water is at the top edge of each frame. A  $\frac{1}{4}$  inch steel sphere, with impact velocity of 3,100 feet per second, penetrated the solution between the vertical rows of hearts and the development of the temporary cavity is seen clearly. The effect on the hearts is described in the text. The vertical row of dots on left are 5 cm apart. The circle in upper left is a mirror reflection of a sodium lamp flashing 170 times a second.

$B_3$ ) were unharmed although hit by shock waves whose peak pressures were about 25 atmospheres, the third heart ( $B_3$ ) was torn and bleeding and its beat slowed. This heart was hit by a 32 atmosphere shock wave but it was also in such a position that rapid radial movement of the water as the cavity expanded and contracted pulled it violently back and forth on its mooring. It is just this same stretching and tearing which must damage tissue around the path of a missile.

The immediate question in this experiment was whether or not it was the shock wave or the tearing which damaged heart  $B_3$ . An attempt was made to answer this question by producing high-intensity shock waves without a cavity or with a minimum of cavity formation. If frog hearts subjected to much stronger shock waves in absence of a cavity are unharmed, we may conclude that movement near the cavity was responsible for damage in the previous experiment.

The experiment was carried out by tying frog hearts in position in a tank of Ringer's solution as before, but rigidly supporting on the surface of the water a  $\frac{1}{8}$  inch thick piece of steel armor plate. This material was then struck with a  $\frac{1}{8}$  inch steel sphere moving 4,500 feet per second. The steel sphere, with a striking energy of  $14.6 \times 10^6$  ergs, did not perforate the armor plate but produced a small hemispherical blister on its undersurface. Spark shadowgrams showed that a strong shock wave arose from the blister and traveled through the liquid. A small cavity also appeared around the blister and quickly subsided. At its maximum this cavity had a volume of approximately 16.7 cc. as compared with the 535 cc. volume of the cavity shown in Fig. 8.

The shock waves from the bulge on the armor plate are shown in Fig. 9. The spherical wave can be seen clearly, as well as the plane waves at an angle of 20 degrees with the plate, which result from elastic waves of the plate. Judging from the width of the absence-of-light band in the spherical shock wave, the peak pressure that struck the hearts (25 cm. away from the plate blister) was between 81 and 117 atmospheres. Despite the greater intensity of shock wave, none of the hearts was injured.

Other similar experiments have led to the general conclusion that shock waves from high-velocity missiles do not damage tissues in a completely liquid system. It therefore seems reasonable to conclude that damage to the heart of the previous experiment was not due to the shock wave but to the rapid movement of water caused by expansion and contraction of the temporary cavity.

#### DAMAGE DUE TO PRESENCE OF GAS POCKETS IN TISSUE

The situation is completely changed when gas is present in tissue. Two of the six hearts suspended under the armor plate and used in the previous experiment each had a bubble of air injected into them with a fine hypodermic needle. The air injection was made some fifteen minutes after the first shot without air injection. This first shot, in which the hearts were not injured, therefore served as a control for the second shot. It was observed that all six (in three different experiments) of these air-injected hearts were injured,

whereas, among a total of seventeen hearts without air injection, exposed to shock waves one, two, or three times, only two were injured and one of these was behaving abnormally before the shot.

Moreover, the nearer the air-injected hearts were to the very small cavity which appeared under the armor plate, the more seriously were they damaged. It was observed in Fig 10, a high-speed moving picture of the air-injected hearts (marked *A* and *F*), that near the cavity a very marked enlargement of

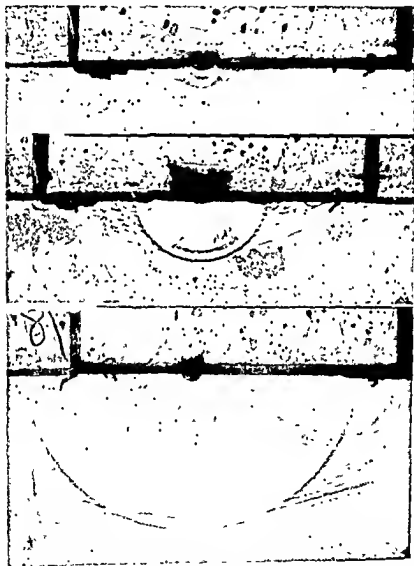


Fig. 9.—Spark shadowgrams (K16, K15 and K14) of the successive movements of a shock wave in water below a  $\frac{1}{2}$  inch sheet of armor plate. The plate has been struck (without penetration) by a  $\frac{1}{8}$  inch steel sphere moving 4 500 feet per second, and the splash of metal is clearly seen. In addition to the hemispherical wave, elastic waves in the metal pass to the water, making an acute angle with the plate.

heart *A* occurred, due to expansion of the air during the sub-atmospheric pressure phase of cavity formation.

Similar expansion of air-filled balloons also occurred near the cavity, as shown in Fig. 11. Balloon *A*, near but never touched by the growing cavity, actually expanded to the bursting point and also affected its neighbor, *C*, below to the left. Balloon *D*, on the other hand, only 6 cm away from the maximum limit of the cavity, was not affected. Balloon *E* received a very strong shock wave, the effect of whose pressure is just perceptible in its slightly smaller size in Frame 1 as compared with frame 0.

Such experiments as are recorded in Fig. 11 give very conclusive evidence that subatmospheric pressures connected with cavity behavior are the cause of destruction in tissue. A comparison may be made with the bursting of the balloon membrane.

#### SECONDARY DAMAGE TO INTESTINES

Perforation of the intestine is one of the important consequences of injury from underwater blast and is also observed well away from the bullet track after shots through the abdomen of anesthetized cats. Roentgenograms show that the cat intestine contains numerous gas pockets. An experiment was therefore set up in the tank to imitate the conditions of an abdominal shot and particularly to observe what happens to a gas pocket in the intestine. A segment of cat's colon and a small part of the ileum were removed, thoroughly washed with saline solution, filled with Ringer-Locke solution, and the ends tied off, leaving a large bubble of air within. It was suspended in a tank of Ringer-Locke solution in the form of a ring, with the ligatures tied together, and the bubble of air so manipulated that part of the air remained near each end. A  $\frac{1}{8}$  inch steel sphere moving about 3,100 feet per second was then shot into the water through the center of the intestinal loop without hitting any part of the tissue, and a high-speed moving picture of the changes was taken.

Frames from this picture are reproduced in Fig. 12. The position of only one air bubble shows well, that at the right end of the intestine. In Frame 1 the cavity from the shot is quite marked and it will be observed that the air in the bubble is compressed, as indicated by the narrower right end of the intestine. In Frames 2, 3, and 4 the right end of the intestine is expanding and the outline of the bubble is clearly visible. The temporary cavity behind the sphere is still expanding rapidly. In Frames 5, 6, and 7 the bubble again contracts and later undergoes less marked form changes which are quite comparable to the balloons of Fig. 1.

When examined after the shot it was observed that the colon was intact except for a small cavity in the mucosa and submucosa over the bubble. The muscularis layer in this area appeared blistered and wrinkled, having been considerably stretched, but it was not perforated. The contents of the gut, originally clear, had become turbid, presumably because of tissue loosened by agitation and stretching.

Greatest movement in the intestine occurred around the air bubble, whose diameter nearly doubled between Frames 1 and 3. This means a volume increase

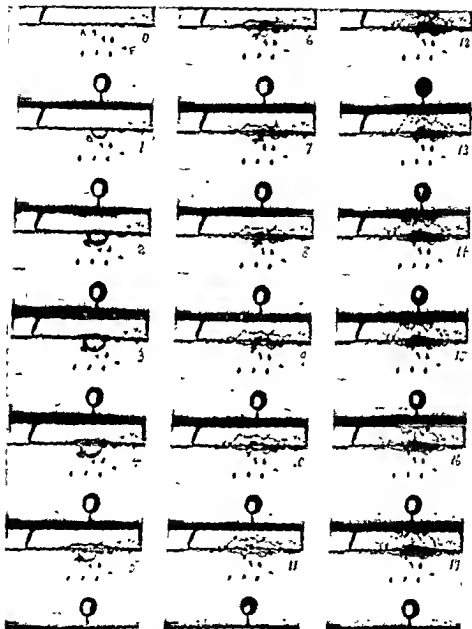


Fig 10—Motion picture (SW3) frames (about 2 000 per second) of six frog hearts tied to horizontal strings (invisible) below a sheet of armor plate, which has been struck (without penetration) by a 14 inch steel sphere moving about 450 feet per second. A small cavity appears under the plate in Frames 1 to 4. The hearts at the upper left and lower right contain air and the expansion of the air in the heart at the upper left is clearly visible. The effect on the hearts is described in the text. The horizontal lines on the left are 5 cm. apart. A circular mirror in the lower middle of each frame reflects a sodium lamp flashing 120 times a second.

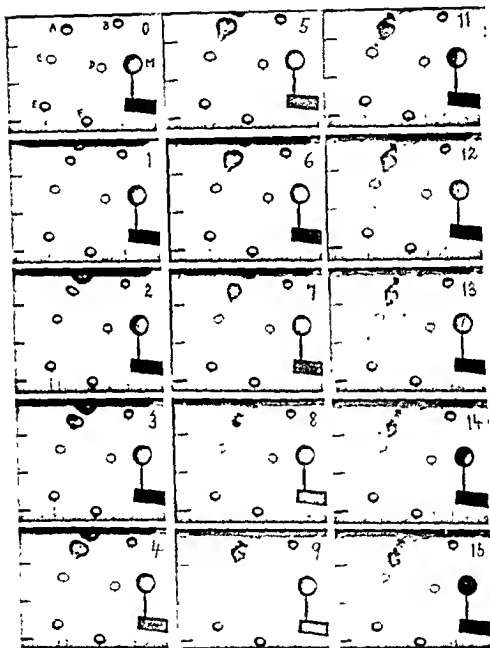


Fig. 11—Motion picture (1981 frames) taken at 2000 per second, of small rubber ball loose filled with air and suspended under armor plate which has been hit by high-velocity sphere. Conditions are the same as shown in Fig. 10. The expansion and bursting of the ball at the upper left as the small cavity under the armor plate approaches is clearly seen. In Figs. 10 and 11 is illustrated how expansion of gas pockets in the body can stretch and destroy tissue. M, marker for timing.

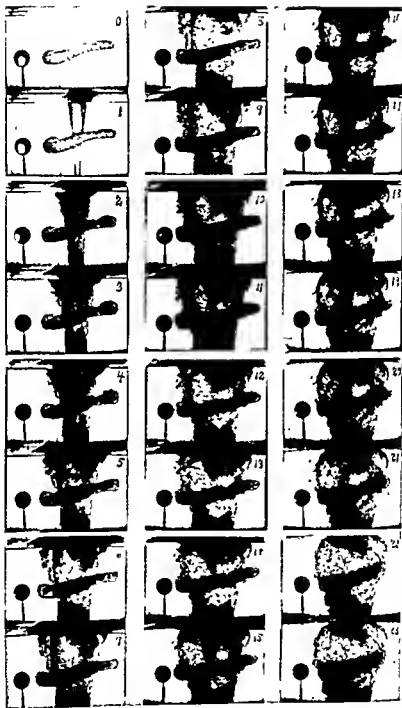


Fig. 17.—Motion picture (173) frames (2,250 per second) of a loop of cat colon with an air pocket in the right end, suspended in a tank of Ringer's solution. A  $\frac{1}{4}$  inch steel sphere with a velocity of 3,100 feet per second entered the water and passed through the center of the loop of colon without hitting it. The large temporary cavity of the air pocket can be seen to expand and the loop of colon. Note especially the slight constriction of the air pocket in Frame 1 and its expansion in Frames 3 to 5. The distance between horizontal lines at the left is 5 cm; the timing mirror is also at the left of each frame.

of eight times in less than one millisecond, since the pictures were taken at 2,280 frames per second. It is not surprising that this rapid stretching should do considerable damage.

The important point which is brought out by the heart and intestine shots is that the stretching is not due to the shock wave proper or to the expanding cavity behind the missile but is due to the expanding air pocket already present within the tissue. The air pocket responds to pressure changes around the temporary cavity and the stretching occurs as a result of subatmospheric pressures clearly visible in the pressure record of the tank of water in Fig. 6. Consequently the damage is to be ascribed to the relatively small long-lasting (measured in milliseconds) pressure changes rather than the short (measured in microseconds) high-pressure pulse of the shock wave.

It is true that the shock wave pressure causes initial contraction of the air mass. When subatmospheric pressure appears the gas springs rapidly from a small to a large volume, thereby causing more rapid stretching, but the fundamental cause of injury is due to great extension of tissue. Pressure change per se does not injure. The displacement of tissue accompanying the shock wave generated by impact of high-velocity steel spheres is invisible in a moving picture and too small to do damage. The displacement from expansion of a gas pocket is readily observed and the damage is comparable to primary damage connected with the temporary cavity.

Where shock waves are enormous, as from underwater explosions of hundreds of pounds of TNT, the displacement in tissue due to the shock wave might be sufficient itself to cause damage. However, the subsequent low pressure around the explosion bubble also extends long distances from the explosion and it may very well be that damage to personnel from underwater explosions is directly connected with the expansion of gas in lung or intestine by this low pressure component. It must also be remembered that whenever a shock wave is reflected from an air surface it is inverted and becomes a low-pressure wave. The reflected wave could also be the important factor in causing damage.

#### SECONDARY DAMAGE TO LUNG TISSUE

Lung hemorrhages occur in personnel injured by underwater explosions. It is not surprising to find that sudden expansion of gas in the alveoli so stretches the walls as to break small blood vessels. No experiments have been carried out to demonstrate damage to lung tissue by a shot in a tank of water, but the report of Daniel<sup>14</sup> of severe lung hemorrhage from gunshot wounds of the skin of the chest is a case in point.

#### DAMAGE TO FISH FROM EXPLOSION AND GUNSHOT

It is well known that fish are particularly sensitive to underwater explosions and can be obtained with little injury by detonating small charges near them. Moreover, hunters have observed that a shot into water near a fish will stun it even though there is no direct hit. The fish lose their power of maintaining equilibrium and are soon found floating at the surface.



Possibly the reason fish are *particularly sensitive* to explosions is again to be sought in their possession of a swim bladder, a mass of gas which is rapidly expanded and injured by the subatmospheric pressure accompanying the cavity formation. We have endeavored to test this view on fish with swim bladders.

In one experiment guppies (about one inch long) were tied to supports in the water and a  $\frac{1}{8}$  inch steel sphere moving 3,100 feet per second was fired among them. All of these delicate fish were killed, although none of them was in the bullet path and many were far removed from the maximum extension of the temporary cavity.

Attempts were made to test this idea further with small goldfish (two inches long) which also possess a large swim bladder connected with the pharynx. By placing goldfish in water under a partial vacuum, the gas of the swim bladder expands and some escapes through the mouth. Roentgenograms of such fish were taken before and after the vacuum treatment to find out how much gas remained. These roentgenograms indicated that the gas volume can be reduced considerably.

Goldfish with a large (before evacuation) and a small (after evacuation) amount of air in the swim bladder were then placed in large mesh hair nets and held in similar positions around the path of a high-velocity shot ( $\frac{1}{8}$  inch steel sphere moving 3,100 feet per second) into water to see if those fish with little air in their swim bladders were unharmed. Because of variability among the fish these preliminary results were inconclusive, although there was some evidence of protection after removal of most of the swim bladder gas. The press of other matters has prevented continuation of these experiments and they should be repeated and extended. It should also be determined whether fish lacking swim bladders (clasmobranch) are immune to secondary explosion damage while those possessing them are particularly sensitive. Enough evidence has been presented to demonstrate the part played by air pockets in wounding.

#### SUMMARY

Primary damage in wounding results from direct crushing of tissue in front of the moving missile and from stretching and tearing in a wide region around the missile path. The stretching results from the formation of a large temporary cavity behind the missile which leaves a region of extravasated blood on collapse. The cavity formation is explosive in character and a comparison is drawn between a shot into tissue and an underwater explosion.

Secondary damage occurs only if gas is present and results from the effect of pressure changes accompanying the passage of the missile through the tissue on the gas. The pressure changes are of three kinds: (1) the shock pressures that originate when the missile strikes and the resulting disturbance in the moving fluid; (2) a high pressure wave moving through the tissue; (3) pressures, both positive and sub-atmospheric, resulting from the behavior of the temporary cavity.

The events which result from firing a shot into tissue are those in tissue. Hence the damage which has been done is due to the pressure changes which result from the shock of the missile striking the tissue and the disturbance in the moving fluid.

suspending tissues or organs in salt solution and shooting among them. Blood corpuscles, frog hearts, and intestinal loops were used.

Damage occurs in gas-free organs only if the tissue is severely stretched by movement of the temporary cavity. When gas is present in an organ, secondary damage results from expansion of the gas as a result of the sub-atmospheric cavity pressure. The expanding gas pocket stretches tissue in a manner quite similar to that of the temporary cavity. Fish in water are peculiarly sensitive to damage from gunfire or detonation because of their swim bladders.

The high pressure of shock waves resulting from impact of missiles does not appear to cause damage; rather, it is decreased pressures that are destructive. Such decreased pressures occur when a shock wave is inverted by reflection from an air surface. In this case the low pressure shock wave can damage. Injury to men in underwater blast probably results from the reflected wave.

#### ACKNOWLEDGMENT

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# THE TREATMENT OF ACUTE APPENDICITIS SUPERIMPOSING SEVERE EXOPHTHALMIC GOITER

I DARIN PUTTELL, M.D., COLUMBUS, OHIO

(From The Department of Research Surgery of The Ohio State University)

**R**EPORTED cases,<sup>1, 2</sup> of exophthalmic goiter complicated by acute abdominal surgical disease have been but few. On the other hand, writers<sup>3, 4</sup> have frequently stressed the importance of differentiating that group of abdominal symptoms of hyperthyroidism such as acute attacks of nausea, vomiting, and pain, which most often simulate acute cholecystitis or acute appendicitis, from actual concomitant acute surgical disease of the abdomen.

In the latter cases the abdominal symptoms are due entirely to overactivity of the thyroid gland, and emergency surgery which is not necessary may lead to disastrous results. Yet failure to recognize and treat properly a concomitant acute appendicitis requiring immediate surgical care may be equally disastrous. Difficulties in differential diagnosis between these two abdominal conditions may at times be insurmountable and clinical differentiation is not always possible. When adequate therapy is applied in hyperthyroidism uncomplicated by an intrabdominal lesion, the abdominal symptoms usually disappear with other signs of toxicity.

In the acute abdominal cases the signs and symptoms usually progress. Moreover, with a concomitant lesion such as acute appendicitis, all of the symptoms and signs of hyperthyroidism may become progressively more severe so that the patient may at times develop a thyroid crisis. A precrisis state is often reached such as that presented by the patient described here, which requires extra preoperative and postoperative care to prevent a thyroid crisis and a fatal issue. In the treatment of this patient the methods set forth in another communication<sup>5</sup> were followed.

## CASE REPORT

A C. (No. 427817), a white housewife 34 years of age, was admitted to the University Hospital on Sept. 12, 1942, at which time there was all evidence of acute appendicitis of four hours' time which had superimposed known exophthalmic goiter of four months' duration.

There was a history at that time of gradual development of a goiter and of nervous irritability since April, 1942, associated with tachycardia, palpitation, emotional instability with easy crying as well as anger without due provocation, decreased tolerance to heat, increased sweating, easy fatigability, muscular weakness, and much loss of weight of from 180 to 175 pounds in spite of a voracious appetite. She claimed these symptoms occurred in attacks which lasted for days without remission and even interfered with sleep. They progressively became worse until July, when they were accompanied by abdominal cramps, nausea, and vomiting. At this time she consulted the local physician who diagnosed toxic goiter. Since 1930 she had several such attacks but much milder with spontaneous remissions. They required no treatment. A basal metabolic rate as determined by the local physician in July, 1942, was increased. He advised thyroidectomy. The symptoms were not relieved by Lugol's solution administered by the physician up to one week before admission.

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During this admission she complained principally of an attack of epigastric cramps which occurred at noon, September 12. It was soon followed by nausea and vomiting. Two hours later the pain localized in the right lower quadrant of the abdomen.

Physical examination revealed the temperature was  $103.4^{\circ}\text{F}$ ., with the pulse 120, respirations 22, and the blood pressure 160 systolic and 90 diastolic. Abdominal examination showed tenderness with slight spasticity in the right lower quadrant over McBurney's area. There was also slight tenderness in the right flank. Rebound tenderness was referred to McBurney's area. The rest of the examination revealed a marked restlessness. The thyroid was moderately and diffusely enlarged. There was moderate exophthalmos. A fine tremor of the protruded tongue and of the extended fingers was present. The face was flushed and the skin warm and moist. Tachycardia, increased pulse pressure, and fever were great. The white blood count was 11,000 with 88 per cent neutrophils and 12 per cent lymphocytes. The urinalysis was negative.

There was an exaggeration of all thyrotoxic symptoms with pending thyroid crisis due to an acute retrocecal appendicitis. Rigorous treatment to prevent thyroid crisis was immediately instituted including adequate sedation, parenteral administration of Ringer's solution with 5 per cent glucose and 500 mg. of iodine as potassium iodide. Emergency appendectomy was performed, September 12. Under avertin, 80 mg per kilogram, and cyclopropane, oxygen, and helium anesthesia, the abdomen was opened through a Battle pararectus incision. An acutely inflamed appendix was found retrocecaly, which was removed. It was gangrenous up to 1 cm. from its base. The stump was treated with phenol and alcohol.

It was not inverted but completely covered with a portion of the mesoappendix. Ten grams of sulfathiazole powder were placed about the appendiceal area. Microscopic examination revealed acute diffuse suppurative appendicitis with areas of gangrene (Fig 1).



Fig 1—Acute suppurative appendicitis. Note the areas of necrosis of the mucosa and the polymorphonuclear cell infiltration of the depths of the appendix.

Immediately following the operation the preoperative measures were continued. Oxygen was administered by intranasal catheter. The body temperature was controlled by an ice-cooling system which consisted of placing over the lower extremities wet towels covered with ice over which air from an electric fan was blown. Morphine,  $\frac{1}{4}$  gr., was given every four hours as long as the respirations were 16 or above. The patient was kept in a semi-Fowler's position. The cooling system was discontinued in a few hours. The postoperative temperature reached its peak of  $101.2^{\circ}\text{F}$  on the first day with the pulse 118 and respirations 24. It gradually returned to normal on the third day, where it stayed thereafter. Sips of water and food were given as soon as tolerated. Two hundred milligrams of iodine as well as a high carbohydrate, high protein, high calcium, high phosphorus, and high vitamin intake were given daily. Recovery was uneventful.

The basal metabolic rate determination on the tenth day, September 22, was plus 22 per cent with the pulse rate 64 and the respirations 11. She was discharged on September 27, the fifteenth day, as improved to return in one month for thyroidectomy. She was advised to continue bed rest, sedation, and a high caloric, high vitamin, high calcium, and high phosphorus diet for a period of one month, during which iodine was discontinued. She

felt well for one week after discharge. Then she began to notice a return of all of the thyrotoxic symptoms. These symptoms became progressively worse until readmission on Oct. 28, 1942. Weight had remained stationary at 135 pounds.

Except for this present illness, general health was good. A left otitis media developed in 1920 with spontaneous rupture of the drum. The upper teeth were all extracted years before because of dental caries. She had short periods of amenorrhea since 1930. Dizziness and frontal headaches occurred occasionally.

Family history revealed no positive findings. She knew of no goiter in the family.

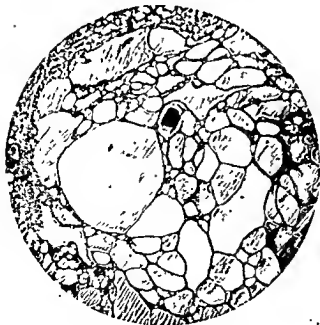
Physical examination revealed a well developed and fairly well nourished white woman whose facial expression was that of frozen terror. Temperature was 98.6° F. with the pulse 140, respirations 28, and the blood pressure 162/90. Face was flushed. Skin was warm and moist. There was marked exophthalmos bilaterally with exophthalmometric readings of 23 mm. on the right and 21 mm. on the left. A widening of the palpebral fissures was demonstrable. There was a lag of the upper lids as the eyes followed the finger downward. Difficulty in convergence was present. Pupils were regular, equal, and reacted well to light and accommodation. The fundi were normal. Hearing was good and the drums intact. There were no nasal abnormalities. She wore a full upper dental plate. The protruded tongue showed a fine tremor. The oropharynx was clear. Indirect laryngoscopy showed the vocal cords normal in appearance and their function good. The neck veins pulsated rapidly and vigorously. There was moderate diffuse enlargement of the thyroid gland. This moved on deglutition. A thrill was palpable and a bruit was heard by auscultation over the gland. Chest and breasts were well developed. Lungs were clear to percussion and auscultation. Heart was not enlarged, its sounds were of good quality, and its rate was rapid but regular. No murmurs were heard. Abdomen showed a well healed right rectus scar. The abdominal wall was soft and not tender. The liver, spleen, and kidneys were not palpable. No masses were found. Pelvic examination disclosed a moderately eroded cervix. The uterus was anteflexed, nodular, and slightly enlarged. Rectal examination revealed small external hemorrhoids. There was a fine tremor of the extended and abducted fingers. The extremities were otherwise normal. Reflexes were slightly hyperactive.

Red blood count at time of admission was 4,770,000 with the hemoglobin 14 Gm. per cent. The white blood count was 5,500 with neutrophiles 53 per cent, lymphocytes 45 per cent, and monocytes 2 per cent. Urinalysis was negative. Blood Wassermann and Kahn reactions were negative. Blood urea nitrogen was 15 mg. per cent. The basal metabolic rate was plus 64 per cent with the pulse 144 and respirations 18. The total blood iodine was 12.26  $\mu$  per cent and the organic fraction 2.64 per cent, which are definitely increased. An electrocardiogram revealed sinus tachycardia and slight left axis deviation. Fluoroscopy and anteroposterior as well as lateral roentgenograms of the neck and chest revealed anterior displacement of the trachea. The lung fields were clear and the heart as well as the aorta appeared normal.

A regimen of adequate bed rest, adequate sedation, and a high calcium, high phosphorus, high vitamin, and high calorie diet was followed. The diet was supplemented with diel D wafers, five daily, for the first fourteen days. On this regimen the basal metabolic rate decreased gradually to plus 40 per cent on November 10 with the pulse 116 and respirations 18. One hundred milligrams of iodine as potassium iodide were given daily beginning on November 12. The basal metabolic rate further decreased to minus 1 per cent with the pulse 96 and respirations 12 on November 24. On this regimen all thyrotoxic symptoms gradually decreased in severity. The patient became generally composed, comfortable, and at ease. There was a gain of weight. She was therefore considered ready for bilateral subtotal thyroidectomy. Morphine,  $\frac{1}{4}$  gr., and scopolamine,  $\frac{1}{60}$  gr., were given preanesthetically. Usual skin preparation with tincture of mercuriochrome and usual draping were made.

Under avertin, cyclopropane, ether, and helium anesthesia, a high collar incision was made. The upper and lower flaps were then dissected back and a midline incision was carried down to the isthmus of the thyroid, thus separating the strap muscles. The right lobe of the thyroid was then exposed and found to be moderately enlarged and principally extended retrotracheally. There was no evidence of nodularity. The left thyroid lobe was

A



B

Fig 2.—A, Exophthalmic goiter. Alveoli are irregular in size, contain a small amount of colloid, and the epithelium is hyperplastic in character with a few papillary projections present. B, Exophthalmic goiter. Small areas of involution such as this were found rarely.

exposed, which was diffusely enlarged. A large part of this lobe was also retrotracheal in position. It was debrided. The upper pole, and then the lower pole, were clamped, divided, and ligated in the usual fashion. The lobe was subtotally excised, using a modified Halsted technique. The right lobe was similarly excised. A pyramidal lobe was totally removed. About 5 Gm. of the posteromedial portion of thyroid gland was left bilaterally. Usual saline irrigation and complete hemostasis using black silk were carried out. Closure was made in the usual fashion using black silk throughout and no drainage. The immediate postoperative condition was excellent.

The thyroid gland as removed weighed 45 Gm. and measured 6 by 2 by 2.5 cm. It was diffusely enlarged, friable, and vascular. On cut section the surface was beefy and uniform in consistency. The amount of colloid appeared minimal. Microscopic examination showed diffuse hyperplasia (Fig. 2, A) with few areas of hyperinvolvement of the acini (Fig. 2, B).

Final diagnosis was genuine exophthalmic goiter.

Postoperatively the patient was placed in a semisitting position. An ice collar was tied about the neck. Fluid and mineral balance were maintained by parenteral administration of Ringer's solution with added 5 per cent glucose and 200 mg. of iodine as potassium iodide. Sips of water were allowed as desired and a rapidly increasing diet was given as tolerated. One hundred milligrams of iodine as potassium iodide were given by mouth on the second day and daily thereafter. The postoperative course was smooth. The temperature reached its peak of 101.3° F. on the first day with the pulse 132 and respirations 22. They rapidly receded and remained normal after the third day. There was never evidence of parathyroid tetany or of recurrent nerve injury. Alternate skin stitches were removed on the second day and the remainder on the fourth day. She was discharged as improved on the fifth day, Nov. 30, 1942.

She was seen by me on Jan. 3, 1943, at which time the basal metabolic rate was plus 3 per cent with the pulse 50, respirations 18, and blood pressure 140/84. She had taken one tablet of iodine (about 10 mg. of iodine) once daily during the interval. There was a gain of weight to 150 pounds and she felt fine. The scar was minimal. The patient was discharged as recovered, to return if symptoms recurred.

# SUMMARY

This case is set forth as presenting a rare complication of exophthalmic goiter. It also emphasizes the minimal postoperative reaction which may occur following emergency appendectomy in the presence of severe exophthalmic goiter.

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# MALIGNANT SOFT TISSUE TUMORS OF THE LOWER EXTREMITIES: A RADICAL-CONSERVATIVE TECHNIQUE OF WIDE EXCISION AND SKIN GRAFTING WITHOUT AMPUTATION

## REPORT OF FIVE CASES

WILLIAM H. MULLER, JR., M.D., and HENRY N. HARRIS, M.D., BALTIMORE, MD.  
(From the Department of Surgery, Johns Hopkins University Medical School and Hospital)

THE purpose of this discussion is to present a method for dealing surgically with certain malignant tumors involving the soft tissues of the lower extremities. This method can be termed a radical-conservative technique: radical in that such an extensive excision is done that large skin grafts are necessary, conservative in that amputation is not performed. It should be stated definitely at this time that we are not advocating this technique as a substitute for amputation nor do we believe that it will give as high a percentage of cures as will amputation. It is, however, indicated in certain cases, particularly when amputation is refused, and is in all instances preferable to a conservative local excision. While the method may be applied in selected cases to any type of malignant neoplasms, it is felt that it can best be used for the slow-growing types of sarcomas. The lower extremities have been chosen for two reasons. The first is that tumors involving this region may be evaluated more accurately concerning their local growth and the infiltration of surrounding tissues, and their regional metastases may be demonstrated more easily. The second is that in all patients upon whom this method has been carried out the location of the tumor was on the lower extremity and the patients with such lesions are often unwilling to have amputation. Since these cases were reported, this technique of radical excision and skin grafting has been applied\* to a superficial sarcoma of the left forearm in a 32-year-old man. Two of our patients refused amputation. The group of slow-growing sarcomas such as the fibro-, myxo-, and liposarcomas make up a relatively small group of malignant neoplasms. However, because they are slow growing, infiltrate locally, and are slow to metastasize, they lend themselves to surgery with potentially very gratifying results, and it is upon these characteristics that the method to be presented here, of very wide excision with extensive skin grafting, is based.

Nothing can be added to the pathologic description of sarcomas as a whole by Ewing<sup>1</sup> and Warren and Sommer.<sup>2</sup> These tumors, in general, are thought to be derived from connective tissue or mesothelial elements. Their cells are laid down upon an abundant vascular network which gives them a highly vascular gross appearance. They may grow quite rapidly, such as either Ewing's or osteogenic sarcomas, or they may grow slowly as does the group with which we are chiefly concerned. If their course is uninterrupted they may reach very large proportions, and when doing so they frequently ulcerate or their centers become necrotic. With the exception of lympho- and melanosarcomas they are thought to metastasize via the blood stream and rarely do they involve regional lymph nodes. However, it was more recently claimed by Ewing,<sup>1</sup> and by Meyer.

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\*By Dr. Bruce Frank.



ding, Broders, and Hargrave,<sup>3</sup> that the regional nodes are involved more frequently than had heretofore been thought, and an incidence of such involvement of 3 to 12 per cent was reported by various authors in the literature. The tumors usually appear to have a capsule which, however, has been shown in most instances not to be a true one because tumor cells may be found in the surrounding tissues. On cut section sarcomas are usually highly cellular, and may be quite firm or soft. Microscopically they present many different cell types. In a series reviewed at the Johns Hopkins Hospital from 1935 to 1945 there were 8 fibrosarcomas, 2 fibromyxosarcomas, 3 neurogenic fibrosarcomas, 1 fibromyxochondroma, 1 spindle-cell, 1 myxo-, 1 macrophage, 1 rhabdomyomyxo-, 1 round-cell, 1 mixed cell, and 1 undifferentiated sarcoma. Warren and Sommer<sup>4</sup> stated that the presence of giant cells is of value in determining the patient's prognosis, while Carroll and Martin<sup>5</sup> in their series found this to be of no significance. The tumor cells frequently are seen invading blood vessels, and they tend to extend along the fascial planes.

The idea of radical-conservative therapy in the treatment of malignancies of the lower extremities is not unique here. Phemister,<sup>2,6</sup> of the University of Chicago Clinics, has written extensively upon minimal surgery of bone tumors involving the long bones. He reported excision of even the highly malignant Ewing's or osteogenic sarcomas followed by bone grafting with excellent results. His cases, however, were highly selected and only the patients in whom a very early diagnosis was made were treated in this manner. It would seem that soft tissue tumors would be far more amenable to radical-conservative therapy than would those involving bone. The fact that they are more cutaneous, and make themselves apparent early, enhances an early diagnosis which is essential to favorable results with any type of treatment.

There is some difference of opinion as to the proper method of treating such neoplasms. The tendency is toward local excision although amputation is advised by some. Bick<sup>7</sup> advocated local excision, to be followed by amputation if there were a recurrence. It would seem that due to the relatively benign characteristics of the tumors a wide local excision would be the treatment of choice. The method employed here is based upon these characteristics and is as follows:

*Technique.*—An incision is made about the tumor in such a manner as to include a very wide margin of skin. The greater width should be proximal to the tumor in line with the direction in which metastasis might take place. It is important to remove a wide margin of skin, especially when excising such tumors as melanomas or others which might actually involve the skin. The incision should extend through the subcutaneous tissue and an even larger area of fascia should be removed. If the tumor involves the muscles, those groups of muscles should be ablated to an equally radical degree. It is particularly important to remove a sufficient area of fascia, because it is along this structure that extension of the tumor tends to take place. If at any time during the procedure there is doubt in the mind of the operator as to whether or not total extirpation of the tumor-bearing tissue is being carried out, a frozen section is of value in confirming this. If it is found that such structures as the

sciatic nerve or great vessels are intimately involved in the tumor, amputation is indicated. Since a large area of skin has been excised, it must of necessity be replaced with a skin graft. As with any plastic procedure this may be done at any time, but the optimal time is at that of the initial procedure because then the wound is fresh and free from infection. Probably the ideal type is the split-thickness dermatome graft because a large area of skin may be obtained with relative ease. Furthermore, the introduction of the dermatome in 1939 has enabled the general surgeons who treat the majority of these tumors to use this technique more readily. In most cases a dissection of the inguinal glands is probably unnecessary. However, if the tumor is one of those which not infrequently metastasize to this region, then this additional procedure should be performed. Postoperative x-ray therapy upon most of these lesions is of little value.

The cases of soft tissue, lower extremity sarcomas reported at the Johns Hopkins Hospital during the ten-year period from 1935 to 1945 have been reviewed. Only those cases which were proved by biopsy were selected and a total of twenty-two were found, exclusive of the cases reported in detail in this paper. The follow-up is of small value because there is little information in most of the records after the patients were discharged from the hospital. However, there are points of interest in the series which will be discussed briefly. In Table I it is noted that the oldest patient was 74 years of age, the youngest 10, and the average 48.2 years. Fifty per cent were between the ages of 40 and 60 years, 10 were males and 12 females, and 19 were white while only 3 were colored. It will be noted that there is a wide variety of types which have been previously listed. It should be emphasized that these tumors are not difficult to diagnose and in all but five cases the preoperative diagnosis was sarcoma. One which had progressed very rapidly over a period of less than one month was thought to be a low-grade cellulitis and gave a clinical appearance of the same. It is the general opinion that trauma plays a prominent part in the initiation of sarcomas. However, only four of the patients (17 per cent) in this series presented such a history, three having previously sustained blows, while in one the tumor had developed at the site of a blister. Meyerding, Broders, and Hargrave<sup>3</sup> reported a history of trauma in 32.9 per cent of their cases, while Carroll and Martin<sup>4</sup> had an incidence of only 5 per cent. It is of interest to note that the presence of a mass or swelling of the part was the only symptom present until late in the course of eighteen cases. Initial pain was present in only two cases, numbness was observed in one case in which the tumor involved the sensory nerves, and stiffness in one in which the tumor was in the popliteal fossa in close apposition with the knee joint. The longest duration of symptoms was eight years, while the shortest was one month, and the average duration was about three years. Carroll and Martin<sup>4</sup> showed a definite relation between the duration and percentage of cures. Those patients in whom the tumor had been present for a long time had a much higher incidence of cure than did those in whom the tumor was of short duration. Of the twenty-two cases, eight patients had had previous excisions of which four were multiple. This is in-

ding, Broders, and Hargrave,<sup>7</sup> that the regional nodes are involved more frequently than had heretofore been thought, and an incidence of such involvement of 3 to 12 per cent was reported by various authors in the literature. The tumors usually appear to have a capsule which, however, has been shown in most instances not to be a true one because tumor cells may be found in the surrounding tissues. On cut section sarcomas are usually highly cellular, and may be quite firm or soft. Microscopically they present many different cell types. In a series reviewed at the Johns Hopkins Hospital from 1935 to 1945 there were 5 fibrosarcomas, 2 fibromyxosarcomas, 3 neurogenic fibrosarcomas, 1 fibromyxochondroma, 1 spindle-cell, 1 myxo-, 1 macrophage, 1 rhabdomyomyxo-, 1 round cell, 1 mixed cell, and 1 undifferentiated sarcoma. Warren and Sommer<sup>8</sup> stated that the presence of giant cells is of value in determining the patient's prognosis, while Carroll and Martin<sup>9</sup> in their series found this to be of no significance. The tumor cells frequently are seen invading blood vessels, and they tend to extend along the fascial planes.

The idea of radical-conservative therapy in the treatment of malignancies of the lower extremities is not unique here. Phemister,<sup>10</sup> of the University of Chicago (Ill.), has written extensively upon minimal surgery of bone tumors involving the long bones. He reported excision of even the highly malignant Ewing's or osteogenic sarcomas followed by bone grafting with excellent results. His cases, however, were highly selected and only the patients in whom a very early diagnosis was made were treated in this manner. It would seem that soft tissue tumors would be far more amenable to radical-conservative therapy than would those involving bone. The fact that they are more cutaneous, and make themselves apparent early, enhances an early diagnosis which is essential to favorable results with any type of treatment.

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previous excisions. Postoperative x-ray treatment was instituted in eleven of the cases, the results of which are not known. The follow-up is quite incomplete. The patient with the round-cell sarcoma lived for five years three months. One with an unidentified and one with a fibrochondromyxosarcoma died at the end of two years, one died on the twentieth postoperative day of a pulmonary embolism, and two were well after four years.

#### CASE REPORTS

**CASE 1**—J. G., a 27-year old white man, was admitted to the hospital Nov. 29, 1944, stating that four years previously, in 1940, he struck the left leg against the emergency brake of an auto, and about three months later noticed a swelling at the site of injury just below the knee. In eight months it had reached the size of an egg and was incised. The lump remained and grew at a moderate rate until about one year later, when it was three times this size and was excised. Six months later it reappeared and grew more rapidly. About two months prior to admission the ankle began to swell on standing. He had lost no weight.



Fig. 1—Grafted area on medial surface of left leg. Patient J. G. Final result fourteen months after radical-conservative excision of recurrent fibrosarcoma.

Physical examination showed a multilobular, firm, bluish red mass on the inner aspect of the left leg elevated 5 cm. above the surrounding surface and measuring 12 by 13 cm. There were two well healed scars over it. No palpable inguinal lymph nodes were felt. On Dec. 2, 1944, the lesion was biopsied and a pathologic report of fibrosarcoma was obtained. The patient was offered a supracondylar amputation but refused. Thus as an alternative a very wide excision of the tumor mass was performed, removing skin, subcutaneous tissue, fascia, and muscle down to the tibia over the medial and anterior and posterior aspects of the leg from about 20 cm. above the medial malleolus and extending upward about 10 cm. on the thigh. The excised tissue, including the tumor and surrounding normal tissue, weighed 1,075 Gm. The area was so large (118 sq. m. as determined by measuring the tracing with a planimeter) that only about two thirds of it was covered with three split thickness dermatome grafts at this time. The postoperative course was uneventful, and six days later the remaining portion was covered with two dermatome grafts in a similar manner. All of the grafts

TABLE I. ANALYSIS OF TWENTY TWO CASES OF SOFT TISSUE SARCOMAS OF THE LOWER EXTREMITIES AT THE JOHNS HOPKINS HOSPITAL, 1935-1945

Age incidence	Oldest, 74 yr. Youngest, 10 yr. Average, 48 yr. 50% between 40 and 60 yr.
Sex	Males, 10 Females, 12
Race	White, 19 Colored, 3
Pathologic type	Fibrosarcoma, 6 Neurogenic fibro-sarcoma, 3 Sarcoma, 2 Fibromyxosarcoma, 2 Spindle cell sarcoma, 1 Macrophage sarcoma, 1 Myxosarcoma, 1 Rhabdomyosarcoma, 1 Round cell sarcoma, 1 Mixed cell sarcoma, 1 Unidentified sarcoma, 1
Preoperative diagnosis	Sarcoma, 14 Benign tumor, 5 Cellulitis, 1
History of trauma	Blow, 3 Blister, 1
Initial symptoms	Presence of a mass or swelling, 18 Pain, 2 Numbness, 1 Joint stiffness, 1
Duration of symptoms	Longest, 8 yr. Shortest, 1 mo. Average, 3 yr.
Location	Thigh, 13 (rt. 8, lt. 5) Leg or foot, 9 (rt. 5, lt. 4)
Previous operation	Excision, 8 (multiple, 3)
X ray findings	Lung metastases, 2 Excision of adjacent bone, 3
Metastases by physical examination	Enlarged inguinal lymph nodes, 2 Abdominal mass, 2
Operation	Biopsy only, 5 Amputation, 6 Local excision, 11
Postoperative x ray	11
Duration of cure (6 cases followed)	Round cell sarcoma, died 3 yr. 3 mo. Fibrosarcoma, living and well 4 yr. Unidentified sarcoma } died 2 yr. Fibrochondromyxosarcoma } Mixed cell sarcoma, died 8 mo. Neurofibrosarcoma, died 20 days after operation of pulmonary embolus

dicative of the fact that inadequate excisions were performed, and it is the desire of the authors to emphasize particularly this point. Frequently the neoplasms appear to be encapsulated and may be shelled out with ease, but tumor cells are left behind in the surrounding tissue and are responsible for the recurrence. It is because of this that the previously described radical excision is recommended. Of the total number of cases, six patients had biopsy only, nine had local excision, and six had amputations. Of the latter six, two had had

CASE 3.—W. H., a 51-year old banker, first entered the Johns Hopkins Hospital on May 29, 1946, with the complaint of a nodule on the inner lower right thigh which had been biopsied elsewhere three days before with the finding of spindle-cell sarcoma. The patient had noted the lump for six weeks. A radical conservative operation was suggested (after consultation with two other surgeons) and in this the patient readily agreed, so it was performed on June 3, 1946.

An oblique incision was made below the inguinal crease on the right and extending medially and downward for about six inches. Through this incision the inguinal and femoral lymph glands and the entire upper end of the saphenous vein were removed. The lower end of the incision joined a circular excision around the previous wound with a margin of about three inches on all sides. This circular excision was 19 cm. in diameter and was done with the cautery down to and including the muscular fascia. The entire length of the gracilis and sartorius muscles beneath the circular excision was removed in one block with the superficial tissues. At no point was the original wound opened into or were tumor or edematous tissues seen. The femoral vessels lying in Hunter's canal were somewhat exposed by the muscular excision, and lay at the extreme lateral side of the wound. To cover them up, a relaxing incision was then made 11 cm. to the right of the circular wound and the edges of the latter were brought closer together by suturing them to the muscular fascia. The resultant defect was then only 12 by 16 cm. instead of 22 by 19 cm. as it had been before partial closure. A single dermatome graft was then taken from the lateral surface of the right thigh and applied to the relaxing incision and to the circular defect. The relaxing incision had allowed the main flap to be brought over to cover the femoral vessels which had been exposed in Hunter's canal. An elastic compression bandage and a plaster cast were then applied. The specimen showed an incomplete original removal, but no spread of the tumor.

The patient was discharged on the seventeenth postoperative day with the wounds and the grafted areas almost healed. He played golf soon after and when last seen six and one half months after operation showed no sign of recurrence. There was little loss of function in the right leg and only a slight pitting edema on the inside of the right ankle, but a swelling was not demonstrable on actual measurement.

CASE 4.—D. S., a 15 year old colored schoolgirl, was first admitted to the Johns Hopkins Hospital on Oct. 11, 1946, complaining of a painful lump on the upper medial aspect of the right calf. This lump had been present for eighteen months, two months before admission had started to grow more rapidly, and one week before admission had begun to discharge bloody material. Examination revealed an ulcerated mass 7 cm. in diameter which protruded 4.5 cm. above the surface.

On Oct. 15, 1946, a fairly radical excision of the mass was performed. A large elliptical incision was made about the tumor with a two inch margin below, and a greater margin above. The fascia of the gastrocnemius muscle was removed with the tumor. It was then noticed that there was a 1 by 2 cm. extension of the tumor at the center of the wound into the outer surface of the gastrocnemius muscle, so a portion of the muscle was removed. A dermatome graft was then taken from the opposite thigh and sutured into the defect. At the same time, the right femoral lymph nodes were excised through a separate incision.

The pathologic examination revealed a localized endothelial sarcoma, probably of a radio-sensitive type. The femoral lymph nodes showed no metastases. The patient was discharged from the hospital on the fifteenth postoperative day with the wounds and the graft almost entirely healed. She was given roentgen therapy to the right groin (3,000 R) and when last seen three months after operation showed no signs of recurrence, but there was some swelling of the leg below the grafted area.

\*By Dr. Hixie Franz

remained viable, and the patient was discharged on Jan. 6, 1945, with only a few small granulating areas. After that time he progressed very well. There was no evidence of recurrence or metastases when last seen twenty-four months after the operation, and the only difficulty was mild occasional swelling of the leg below the excision when standing for long periods of time.

**CASE 2—M S J**, a 38 year old housewife, first entered the Johns Hopkins Hospital on Feb. 18, 1942, with the chief complaint of progressive enlargement of a mole on the inner aspect of the lower left leg. Family history and past history were not remarkable. As far as the patient knew the mole had been present all her life, and in July, 1941, it began to become suddenly larger, until admission on Feb. 18, 1942.

Physical examination showed a hard, bluish, hairless, raised area about 2 cm. in diameter. About it were many similar areas measuring approximately 2 to 4 mm. over a radius of about 5 cm. There were no enlarged inguinal nodes.

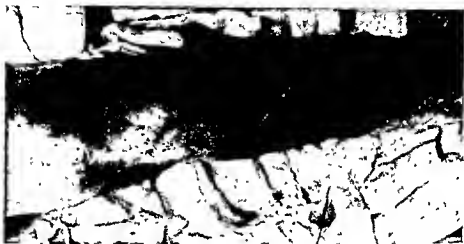


Fig 2—Grafted area on medial surface of left leg, Patient M. J. Result on twelfth day after excision of recurrent malignant melanoma.

The area was excised and a single full thickness graft applied. The patient was discharged on March 13, 1942, and the area was healed. The course was uneventful until February, 1945, when she noticed a small dark nodule in the center of the graft. This nodule began to grow rapidly, and several months later a similar nodule appeared in the skin about 10 cm. above the first and then another about 10 cm. above the second. She had lost about twenty pounds in weight.

Physical examination revealed a bluish mass about 4 by 2 cm. in the graft, and two similar lesions 2 by 1 cm., and about 10 and 20 cm., respectively, above the first. Several smaller, moderately firm inguinal nodes were felt. The chest was clear by x ray examination. The patient refused amputation, and on Oct. 18, 1945, a radical excision and skin grafting were performed. This excision removed the skin, subcutaneous tissue, and fascia over the entire medial aspect of the leg and the thigh to just above the knee. On October 25 a radical excision of the left inguinal glands was performed. The patient was discharged with the grafted area almost entirely healed on Nov. 12, 1945. She had a recurrence proved by biopsy below the grafted area in September, 1946, following which a Callender amputation was done on Sept. 25, 1946. When last seen four months later she showed no sign of recurrence. Although this type of tumor is not suited for this procedure, it was performed only because the patient would not originally agree to amputation.

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CASE 5—E. C., a 36 year old colored divorced woman clerk, first entered the Johns Hopkins Hospital on Aug. 21, 1946, complaining of a lump on the lateral surface of the right hip of two years' duration. This lump began to grow more rapidly six months before admission, attaining the size of a small orange. The lump had bled slightly for one week, but was painless. It projected about 3 cm. above the skin surface.

On Aug. 23, 1946, the lump was excised\* by an elliptical incision, the anterior portion of which lay along the iliac crest. The fascia overlying the gluteus maximus muscle was removed with the tumor. A dermatome graft was applied to the defect, which measured 16 by 10 cm., four months after operation after the contracture of healing had occurred. Small deep grafts were applied to a small unhealed area on Sept. 16, 1946, and the patient was discharged two weeks later.

Pathologic examination revealed a well-encapsulated lump 4 cm. in diameter which showed a structure typical of neurogenic sarcoma on microscopic examination. When last seen five months after discharge the patient showed no sign of recurrence.

#### COMMENT

It is fully realized that the report of only five patients with such a short postoperative follow-up can lead to few definite conclusions. One of the five patients (Case 2) developed a recurrence and the leg was amputated eleven months after the radical-conservative operation. However, as has been previously pointed out, the general tendency is toward an inadequate local excision of such tumors. Since many of these patients refuse amputation, the choice is often not between radical local excision and amputation, but between radical local excision and conservative local excision. Because of the relatively benign characteristics of local growth and infiltration and late metastasis to other regions of these tumors, and because they are now infrequently deceptive by their false capsules, we wish to point out that local removal will give good results in selected cases and to emphasize that the excision should be sufficiently radical to eradicate all tumor-bearing tissue. When amputation is refused, this technique, properly applied, is sufficiently superior to conservative local excision to make its performance worth the extra time and trouble.

#### SUMMARY

1. In certain cases of superficial malignant tumors when amputation is refused, an extremely wide local excision with the immediate application of large skin grafts has certain advantages. This method we have termed the radical-conservative method since it does not involve amputation.

2. This technique is the treatment of choice when the patient has refused amputation and may give almost as good results as amputation in so far as a cure is concerned in the management of many malignant tumors, particularly those of lesser malignancy which involve the lower extremities. When vital structures such as the sciatic nerve are involved, the method is contraindicated and amputation should be done.

3. Five cases are presented of the application of the radical-conservative method of dealing with superficial malignant tumors of the lower extremities.

\*By Dr. Bruce Franz

developed by a  $\frac{1}{8}$  h. p. motor at 1,725 r.p.m. (*M*), actuating a high vacuum pump (*VP*), capable of producing a vacuum of 0.0003 mm. of mercury. The rapid intermittent percussions are transmitted to a surge chamber (*SC*) of 1,000 c.c. capacity. The negative pressure (*NP*) is measured by an ordinary U type mercury manometer (*HgM*) and is transmitted to the drainage jar (*D*) by 4 mm. copper tubing. The joints between the metal screw cap and each of its penetrating tubes are soldered for airtightness. The negative pressure developed is maintained at a predetermined level by a mercury valve (*HgV*). This valve consists of an 8 by 1 inch test tube with accurately fitted two-hole rubber stopper, through one opening of which a glass tube, 3 or 4 mm. in diameter and open to the atmosphere at one end, passes through mercury to the bottom of the test tube. A short length of glass tubing passes through the other hole of the rubber stopper and is connected to the suction line between the surge chamber and the drainage jar by 4 mm. copper tubing.

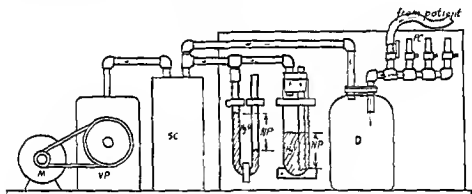


Fig 1.—Mercury controlled suction apparatus. *D*, Drain. *HgM*, mercury manometer, *HgV*, mercury valve. *M*, motor, *NP*, negative pressure. *PC*, pet cocks, *SC*, surge chamber, *VP*, vacuum pump.

To increase the amount of suction, mercury is merely added through the open glass tube of the valve, the degree of negative pressure being equal to the length of the mercury column between the immersed tip of glass tubing and the meniscus. This length is always equal to the difference in height of the mercury columns in the two limbs of the manometer (*HgM*), since greater suction than this will be neutralized by air drawn through the open glass tubing. In operation, therefore, there is a shimmering or bubbling of the upper surface of the mercury in the valve due to the neutralizing air. The effect is to maintain the negative pressure at whatever the effective column of mercury is present in the valve.

The four pet cocks permit the suction to be available for four patients. Whatever cocks are not in use are turned off. With the arrangement described, the patient sleeps without being disturbed, and may sit in a bedside chair during the day, or stand at the bedside, without interfering with the operation of the suction.

## A CONTROLLED SUCTION APPARATUS FOR GENERAL SURGICAL USE

CARROLL J. BELLIS, M.D., LONG BEACH, CALIF.

### INTRODUCTION

CONTINUOUS suction of a predetermined degree is often mandatory in the postoperative care of surgical diseases. Common among such cases are those of thoracic empyema and intestinal fistulas. The principles involved in the surgical treatment of thoracic empyema have been reviewed by Carlson,<sup>1</sup> Connors,<sup>4</sup> Heuer,<sup>12</sup> and Bellis and Churney.<sup>2</sup> Each author has emphasized the importance of early and adequate thoracostomy, within the limitations derived from the investigations of Graham and his students,<sup>4-6</sup> and has stressed the value of suction. At about the third week after the onset of acute empyema, when mediastinal and diaphragmatic stabilization is usually adequate, open thoracotomy may be permitted without embarrassment of the vital capacity due to mediastinal shift. Re-expansion of the lung following thoracostomy is largely a function of the synechiae between the visceral and parietal pleurae, and may be accelerated by continuous suction applied to the thoracostomy tube. To this end, various devices for applying tidal irrigation and suction to the thoracostomy tube have been suggested by d'Abreu,<sup>3</sup> Hart,<sup>10, 11</sup> Wangenstein,<sup>7</sup> Lloyd,<sup>14</sup> Hochberg and Fiore,<sup>13</sup> Neville,<sup>12</sup> Touroff,<sup>16</sup> Weinberg and Sperling,<sup>18</sup> and Bellis.<sup>1</sup>

In the presence of bronchopleural fistula, constant suction applied to the thoracostomy tube is imperative lest the pus be aspirated into the bronchial tree. In the tedious management of intestinal fistulas, the nursing care parallels the nutritional problem in importance. It is well known that stomal narrowing in surgical ileostomy performed for chronic ulcerative colitis or in extra-peritoneal intestinal resection performed for ischemic necrosis or for regional enteritis is enhanced by continuous suction applied to the abdominal surface. The ancillary effects of suction applied to traumatic intestinal fistulas are recognized similarly.

It is the purpose of this communication to describe a controlled constant suction apparatus similar to the one used at the University of Minnesota Hospitals.

### APPARATUS

The tube coming from the patient is connected by a glass or metal Y tube to an additional 2 meters of pressure tubing attached to one of four pet rocks (Fig 1, PC), each having an internal diameter of 8 mm. A common carryoff, 1.5 cm. in diameter, is abruptly turned through the metal screw cap of an ordinary 2,000 c.c. drain jar (D) for receiving the exudate or irrigant. A short length of intravenous tubing is attached to the third limb of the Y tube and clamped shut, being present for intermittent introduction of irrigant and for occasional measurement of the cavity capacity, if used for empyema. Suction is

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After surgical drainage of an empyema pocket has been established by the insertion of a tube with multiple perforations into the most dependent and posterior portion of the cavity, an airtight seal is made at the point of entrance of the tube into the chest. This is done by pulling the tube through a rubber sponge saturated with yellow petrolatum or by surrounding the site with mechanic's waste similarly saturated. Multiple strips of adhesive tape, 6 or 8 cm. wide and 40 to 50 cm. long, further compress the sealing mechanism to insure airtightness. The degree of suction used in empyema depends upon the acuteness of the disease. An early empyema pocket may require 20 mm. of mercury negative pressure, whereas an older pocket with a less elastic visceral wall may necessitate as much as 100 mm. of mercury negative pressure. The degree of obliteration of the pocket may be measured by means of the Y tube. To do this, the motor is switched off and saline solution allowed to run into the empyema pocket by gravity through the extra limb of the Y tube until the liquid overflows. The tip of the Y tube limb is held at the level of the upper limit of the empyema pocket, and the saline solution is never admitted with extra pressure, such as with a syringe, for by so doing, the adhesions formed may be broken and the healing attained nullified. If the exudate is very thick, containing, as it often does, clumps, it may be necessary to dilute it every four or six hours by introduction, in a similar manner, of an irrigant.

The number of dressings required in the case of intestinal fistula is markedly reduced by taping the suction tube to the abdominal skin. Multiple perforations of the rubber tube, which is fixed in place to lie directly over the fistula, permit the drawing off of excretions which may contain particulate material of such dimensions which would occlude a single-hole tube. The apparatus has been found to be invaluable for this purpose.

#### COMMENT

Open or closed drainage, of course, must be deferred in empyema until the synpneumonic stage is over. In the metapneumonic or postpneumonic stage, suction is a definite therapeutic aid. In empyema thoracis, due to conditions other than pneumonia (such as fractured rib with laceration of the lung, gunshot or impalement wounds), the stability of the mediastinum and diaphragm is awaited before establishing thoracostomy. Additional information is given by the cellular content of the pus. However, the establishment of bronchopleural fistula must be considered a surgical emergency, whatever the degree of pleural thickening or density of the pus.

#### SUMMARY

The application of suction to the treatment of empyema thoracis and intestinal fistulas is discussed briefly, and an apparatus for this purpose incorporating a mercury valve for regulating the degree of negative pressure is described.

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quently, field hospitals were located only three to four miles from the front. On several occasions (when the rivers Saar and Moselle were being crossed) because of blown-out bridges and the hazards of fire, it took some of the patients as long as forty-eight hours to arrive at the field hospital.

*Preoperative Management*—It was imperative to improve the general condition of the patients before undertaking definitive surgery. Most of the wounded were admitted in a state of shock, and were immediately taken to a preoperative tent, where the extent of their injuries was evaluated and shock therapy instituted by special shock teams. Patients were prepared for surgery by transfusions of blood, plasma, and serum albumin when available. Blood, which was delivered daily by blood bank trucks, was of utmost value in preparing and fortifying the wounded for surgery. Treatment consisted of restoration of the circulatory blood volume by the rapid administration of blood and plasma, and of serum albumin. Blood was considered decidedly preferable, and the ratio was consistently kept to at least 50 per cent blood of the total of fluids administered. Dependable studies of blood volume losses made in forward hospitals indicate that soldiers seriously injured have averaged a loss of at least one-third of their total blood volume. It has been stated by Cutler that a blood pressure of 85 mm of mercury systolic usually indicates such loss of one-third of the blood volume.

The amount of fluid given varied in each case, depending upon response of the individual patient. A level of systolic blood pressure of at least 100 mm of mercury was regarded as desirable prior to operation. An improvement in pulse volume, indicating an increased cardiac output, was considered almost as important as a rise in blood pressure. Not uncommonly, 3 to 6 L. of fluid had to be administered before the patient could be taken to the x-ray and surgery tent. Very few patients were admitted to the operating tent without having had at least 500 cc of blood administered.

The infusions were given rapidly, and the response to adequate replacement of blood volume loss was often very gratifying. Two or three veins were frequently chosen for simultaneous administration of fluids. The external jugular vein was often utilized by the anesthetist who administered the fluids in the operating room. The femoral vein was occasionally used in emergencies, no other veins being available.

Blood was practically always on hand, and was usually supplied in the form of Alsever's solution (500 cc of blood and 500 cc glucose and electrolyte). It was delivered to the field hospital ten days after it had been drawn in New York or Boston. Cutler, in a recent report, stated that from May 22, 1944, to May 31, 1945, 385,291 pints of blood were used in the European Theater of Operations, 194,712 pints were flown over from the United States.

Serum albumin, when available, was very helpful and useful in combination with blood. The response to 100 cc of serum albumin administered rapidly to a pulseless patient in deep shock was often dramatic.

Shock was further treated by the elevation of the foot of the litter in a modified Trendelenburg position. Oxygen was administered in all cases of se-

## SURGERY OF WAR WOUNDS OF THE ABDOMEN

A REVIEW OF ONE HUNDRED CONSECUTIVE PATIENTS, OPERATED UPON BY A SINGLE SURGICAL TEAM, WORKING IN FORWARD AREAS IN THE EUROPEAN THEATER OF OPERATIONS

LOUIS STERLING, M.D., BEVERLY HILLS, CALIF., LEWIS H. BOSHER, M.D., RICHMOND, VA., AND HAROLD ZIMMERMAN, M.D., EVANSVILLE, IND.

**I**N WORLD WAR II, the mortality from abdominal wounds has been less than ever before. However, penetrating wounds of the abdomen still must be considered as among the most serious casualties of warfare.

The necessity of early operation in cases of penetrating abdominal wounds with visceral damage is now accepted so generally that controversy on this subject which went on before World War I has now completely ceased.

The incidence of abdominal wounds in the European Theater of Operations was 5.2 per cent, as compared with 43.6 per cent for the lower extremities, 2 per cent for the upper extremities, 4.4 per cent for the chest, and 12.5 per cent for the head and neck.

This series is presented to help evaluate the importance of some of the factors influencing the outcome in patients with abdominal injuries. It is a record of part of the experience of a single surgical team, operating in forward field hospitals of the Third Army, in its trek from Normandy through France, Germany, Austria, and Czechoslovakia. A surgical team consists of the surgeon, an assistant, an anesthetist, a nurse, and two enlisted men, traveling as a unit under orders of the army surgeon, to those field hospitals carrying the heaviest load.

Field hospital units were set up to support each division. The capacity of each unit was approximately 50 to 100 patients, and when filled to capacity it was leapfrogged by another similar group. Two surgical teams were assigned to each hospital, each team operating a twelve-hour shift. With the development of a heavy backlog of patients, it often became necessary to reinforce the operating personnel by the addition of more surgical teams.

Since it was necessary to remain mobile, all patients with abdominal injuries were evacuated as soon as they became transportable, which was usually seven to ten days following surgery. Such a period of postoperative stay in the hospital was recommended by the theater surgeon, and was usually of adequate duration.

During periods of stress, with the hospital under shell fire, it sometimes became necessary to evacuate patients earlier. In times of rapid advance, surgical teams were then sent forward to work in the clearing stations, leaving the hospital patients with so-called holding companies.

Treatment of abdominal injuries was definitive in character, and in most instances complete. The majority of patients arrived at the field hospital within from six to twenty-four hours following injury. The time of arrival was, of course, dependent upon many factors influencing the chain of evacuation. Fre-

night, because of hazardous enemy fire. and yet, forty-five patients with abdominal and chest injuries were operated upon by two surgical teams, without a single surgical death. The only death in this group occurred in the preoperative tent, and was due to irreversible shock resulting from bilateral traumatic amputation. Some of these patients were admitted as late as sixty hours after injury. It is likely that those most seriously wounded must have died before reaching the field hospital.

Of the fourteen patients who died, the average lag from injury to time of operation was fourteen hours. Twelve of these were in profound shock upon admission. It is interesting to note that the time lag for all cases in which it was recorded (seventy-two) averaged 15.6 hours, indicating again that the time factor is probably not as important as heretofore assumed.

The extent of injury and the degree and persistence of shock are of such primary importance that the delay of surgical treatment can be regarded as relatively less critical. The danger of infection which is so closely related to the time interval before operation has been considerably reduced as a result of chemotherapy.

*Anesthesia*—Ether was the anesthetic agent of choice. It was administered preferably through an endotracheal tube. The tube affords better control of the respiratory exchange and depth of anesthesia. Opportunity for aspiration of foreign material was thus lessened, and the prevention of postoperative pulmonary complications through easy therapeutic aspiration of mucus and secretions in the bronchial tree was considered important.

The addition of bilateral intercostal block with novocain was found to be helpful in securing relaxation of the abdominal wall and facilitating the operation, especially in those poor-risk patients in whom deep anesthesia was likely to result in a further drop of the blood pressure. Curare was not available, and would probably have been contraindicated under the prevailing circumstances.

*Missiles Producing the Wounds*—The type of missile and the nature of the wound produced have apparently little effect upon the rate of mortality. It is rather the extent of the injury and amount of visceral damage, reflected by shock and hemorrhage, which are the decisive factors. It might be said that abdominal wounds due to mortar fire were the worst seen, in that they were multiple. The through-and-through injuries made by rifle and machine gun bullets were much less severe.

*Incision*.—The location of the wound and the site of the missile and foreign bodies, as indicated by the x-ray examination which helped visualize the course of the projectile, were important factors in planning the incision. For through-and-through injuries in either the right or left upper quadrants, transverse subcostal incisions were utilized as often as possible. Long pararectus incisions were reserved for patients with multiple injuries. Colostomy, when indicated, was usually done through a smaller stab wound, lateral to the incision. Drainage of the peritoneal cavity was deemed necessary only infrequently. The retroperitoneal spaces involved, however, were drained almost routinely. Closure of



vere shock, especially to those patients with associated chest injuries. Large doses of coramine, 10 to 12 c.c., seemed to be of some value in a few cases, when given together with replacement therapy. Patients were not moved, often coming to the operating tent on the same litter on which they were admitted. The patients were operated upon on this litter, and moved only to a cot in the post-operative ward.

A few hours' delay to prepare the patient for operation was found to be justified. Failure of the patient to respond to therapy within two hours, or relapsing shock, usually indicated continuing internal hemorrhage. This necessitated immediate exploration in spite of the risk involved in the presence of shock. Two deaths on the operating table occurred in this group of cases.

Delay between admission and operation was usually not more than two to four hours. Occasional further delay was due to large numbers of casualties admitted within a short period.

Concomitant with the improvement in the general condition of the patient, a careful appraisal of the abdominal injury was made. Wounds of entry and exit were examined. The possibility of missiles entering the abdomen from above through the diaphragm or from below by way of the buttocks, back, or thighs was considered.

As soon as the patient's condition permitted, x-ray examination of the chest and abdomen was made. The chest was x-rayed in every case of abdominal injury and the abdomen in every case of chest injury in order to determine the location of the missiles, to decide whether penetration of the peritoneal cavity had taken place, and to help in planning the operative procedure. Urine examination was done routinely in all cases; whenever the patient was unable to void, catheterization was carried out and in case of hematuria an indwelling catheter was left in place. Hematuria due to kidney or bladder involvement was quite common. Rectal and proctoscopic examinations occasionally revealed previously undiagnosed injuries of the lower bowel.

Every patient admitted for intra-abdominal injury had the stomach emptied by gastric suction before he was taken to the surgical tent. Preoperative gastric suction prevented acute gastric dilatation and diminished the likelihood of aspiration of vomitus, with its dire consequences. At the completion of surgery the indwelling gastric catheter could often be threaded into the duodenum, assuring a smoother convalescence, especially if suture or resection of the small bowel had been performed. The Miller-Abbott tube was successfully used in a few cases of small bowel obstruction which developed during the first postoperative week.

In spite of the fact that the front line was only a very few miles away, the time lag between injury and admission to the hospital was often quite considerable. The average interval for seventy-two cases of which such records were kept was 15.6 hours. This time lag between injury and surgical care has long been considered a major factor affecting the mortality rate. However, that it is not the only decisive element is illustrated by the fact that for a period of about one week (the crossing of the river Saar by the 90th Division) casualties could not be evacuated across the river except at

There were six deaths in cases involving injury to the small gut. The mortality in the cases of resection of small bowel was approximately the same as in those in which closure of multiple perforations was done, in spite of the fact that resection was resorted to only when the extensive injury to the bowel precluded simple closure of the perforations. There were nine resections of the small bowel, with two deaths. In both of these fatal cases the patients were admitted with evisceration; in one there was marked involvement of the terminal ileum and practically complete destruction of cecum and ascending colon. Resection of the terminal ileum and right side of the colon had to be done with ileocolostomy. The defect in the abdominal wall was so great that closure could be accomplished only by substituting a large petrolatum pack for abdominal wall. The patient died two days later of pulmonary complications. The second death following resection of small gut occurred in a patient with extensive injury to the colon as well as to the right arm, with destruction of the brachial artery. The arm had to be amputated. The patient died within twelve hours of irreversible shock.

There were nineteen cases of injuries to the small bowel, in which simple closure of multiple perforations was done. Four deaths occurred. One patient had compound comminuted fracture of the femur, evisceration, and six perforations of the small gut. The second had laceration of the colon, small bowel, and injury to the spinal cord. The third was admitted with fractured femur, ruptured colon, and ten perforations of the small gut. The fourth had ten perforations of the ileum as well as injury to the region of the left ureter.

*Colon.*—In twenty-six cases, injury to the colon was noted. Eight deaths occurred in this group. All of these were associated with severe injuries to other viscera, as small bowel or kidney, or with fractured femur, evisceration, and severe shock. The small bowel plus the colon were injured in four of these fatal cases, kidney plus colon in two cases, liver, stomach, and colon in one case; severe retroperitoneal hematoma and colon in one case. Colostomy was always carried out for injury of the colon, and in cases of injury to the rectosigmoid, the perforations were closed and colostomy performed on the sigmoid for complete diversion of the fecal stream. Colostomy was done routinely for all injuries to the rectum. Massive inundation of the peritoneal cavity with the fluid feces, through multiple perforations of the lower small bowel and colon, especially if associated with massive retroperitoneal hematoma with kidney injury, seems to be productive of severe unremitting shock. This was true of each one of the eight colon cases in which the patient died. The role of massive bacterial spillage in establishing deep shock has recently been emphasized by Jarvis and associates.

TABLE II. MORTALITY AS AFFECTED BY ASSOCIATED INJURY OF THE COLON

ASSOCIATED INJURY	NUMBER OF CASES	NUMBER OF DEATHS	PER CENT MORTALITY
Small bowel injury without colon injury	17	2	11.7
Colon or rectosigmoid injury without small bowel injury	15	4	26.6
Colon plus small bowel injury	11	4	36.3

the incisions was accomplished in layers with interrupted silk, with the addition of heavy retention sutures, spaced about one inch apart to include all layers. The skin was not closed in wounds with marked contamination. Wound infections were not encountered during the seven- to ten-day stay of the patients in the field hospital.

*Extent of Visceral Injury.*—The mortality was directly proportional to the extent of visceral injury. There were 14 deaths in this series of 100 cases, and each of these patients had suffered multiple injuries. The organ most frequently injured among the fatal cases was the colon. Very few instances occurred in which only a single viscus was affected, and no patient in that group died. In the following discussion of abdominal war wounds it should be noted that only multiple injuries affecting several viscera caused the fatal outcome of cases. Each fatal case, therefore, appears in the following under as many headings as viscera were involved.

TABLE I. ORGANS INVOLVED IN 100 CASES (WITH DEATHS LISTED ACCORDING TO ORGANS)

ORGAN	NUMBER OF CASES	NUMBER OF DEATHS
Stomach	7	1
Duodenum	3	1
Small intestine	24	6
Colon	28	8
Rectum	3	1
Bladder	6	0
Gall bladder	1	0
Liver	30	3
Pancreas	1	0
Spleen	9	1
Kidney	19	3
Retroperitoneal hematoma	29	5
Thoracoabdominal	25	3
Negative exploration	6	0
Evisceration	8	2

*Stomach.*—Seven patients were admitted with perforation of the stomach. In each of these, other visceral damage was present, consisting most frequently of liver injury. One death occurred, the wound of entrance in this case being through the right axilla, there was also laceration of the right lung and diaphragm, and of the liver, stomach, and colon. The sucking wound of the right side of the chest was closed, as were lacerations of the stomach at laparotomy; bleeding from the liver was controlled, and the ruptured colon exteriorized. Death occurred on the third postoperative day, from atelectasis and bronchopneumonia.

*Duodenum.*—There were three cases of injury to the duodenum. The stomach and pancreas were also involved in one; the retroperitoneal portion of the duodenum, liver, and stomach in the second. These two patients recovered. A third one, a 65-year-old French civilian woman, had two perforations of the first portion of the duodenum, and lacerations of the liver and the left kidney. She died four hours after operation.

*Small Intestine.*—The small bowel was injured in twenty-eight cases. Multiple perforations were the rule, and as many as fifteen were sutured in a single individual.

kidney and colon injury always seems to be a serious one. Conservatism was the rule, and nephrectomy was carried out only twice in patients in whom exploration revealed the kidney to be ruptured or hopelessly injured. In all cases hematuria disappeared within a few days. An indwelling catheter was left in the bladder until the urine was clear grossly. In no instance was it regretted that nephrectomy had not been performed. The wounds were débrided and liberal drainage was provided for. In conservatively treated patients significant postoperative secondary renal hemorrhage or severe infection did not occur while the patient remained in the field hospital.

*Thoracoabdominal Wounds*.—In twenty-five cases, injury of the chest was associated with abdominal damage. The abdominal involvement was caused either by penetration through the diaphragm or by a separate injury. There were three deaths. One was a case previously mentioned, in which splenectomy was carried out through the chest, the second involved a sucking wound of the right side of the chest with injury to the diaphragm, liver, stomach, and colon, in the third case, the patient had a sucking wound in the left side of the chest, associated injury to the left diaphragm, and had also been wounded in the left kidney and suffered severe retroperitoneal hemorrhage, with complete paraplegia due to spinal cord injury.

The presence of abdominal rigidity, associated with penetrating wounds of the chest and especially with multiple fractured ribs, was noted quite frequently. Usually it was unilateral, and unless examination of the path of the missile revealed intra-abdominal penetration, laparotomy was not done. Acute dilatation of the stomach was a frequent complication of thoracic injury. Decompression of the stomach in these cases was considered essential to improve respiratory exchange.

In the combined chest and abdominal injuries, it was preferred to perform the chest surgery first. It was considered important to stabilize the respiratory exchange, reduce shock, and give the patient the maximum benefit of relief from anoxia, before proceeding with the abdominal exploration. This involved such procedures as relief of tension pneumothorax, aspiration of hemothorax, and closure of sucking wounds.

The common intrathoracic procedures were aspiration of hemothorax, removal of foreign bodies and embedded fragments from the lung, and suture of lacerated lung and diaphragm. In large penetrating and sucking wounds the approach to the upper abdomen through the diaphragm was considered to be most appropriate. Suture of the diaphragm was relatively easy, and exploration of the upper abdomen, splenectomy, etc., was readily accomplished in this manner.

*Negative Exploration*.—In six cases the abdomen was explored with negative findings. No injuries to the intraperitoneal organs were found, and no deaths occurred. These patients, of course, would have fared better without laparotomy, but it was preferable to have erred on the side of intervention rather than to have omitted exploration. In one case, exploration at first also seemed to be negative, until careful search revealed a small perforation at the apex of

*Rectum*.—There were three cases of injury to the rectum. The wounds were débrided. Perforations of the rectosigmoid were closed and abdominal colostomy was carried out. The coccyx was excised for adequate drainage of the retroperitoneal space. No fatalities occurred in this group.

*Bladder*.—In six cases the urinary bladder was perforated. There were no deaths. Four of these patients suffered involvement of the small bowel or colon. Once there was associated compound comminuted fracture of the femur. In only one case was injury to the bladder noted without any concomitant visceral damage.

*Liver*.—Wounds of the liver were encountered in thirty cases. It was the organ most frequently injured. There were three deaths, one from laceration through the porta hepatis, involving severe injury to the liver. Death was due to bile peritonitis. The second was the 65-year old French civilian woman previously mentioned, and involved laceration of the duodenum, left kidney, and liver. The third presented a combination of injuries to the chest, lung, diaphragm, liver, stomach, and colon.

Drainage of the subhepatic and subdiaphragmatic space was carried out routinely when laceration of the liver was present or when laceration of the liver was found during repair of the right diaphragm. No attempt was made to remove foreign bodies which were deeply embedded in hepatic substance. Control of bleeding from liver injury seldom presented serious difficulty. Packing with gauze usually proved sufficient, and suture was performed only infrequently. In one instance, perforations of the gall bladder were closed with subsequent uneventful recovery.

Only one case of direct injury to the pancreas was recorded. There was in that case associated injury to stomach and duodenum. The patient recovered.

*Spleen*.—Severe hemorrhage from rupture of the spleen necessitated splenectomy in five cases. In four other instances of bruises or minor lacerations of the spleen, hemorrhage had ceased and the spleen was not removed. Conservatism in this group seemed justified as no subsequent deaths occurred, and complications due to delayed hemorrhage did not take place. The surgical approach was usually through a left subcostal incision. Transthoracic splenectomy was carried out three times when a left thoracoabdominal wound was present. There was one death in this group. It was a case of left thoracoabdominal injury, a large sucking wound of the left chest with evisceration of omentum, laceration of diaphragm, and ruptured spleen. Profound shock persisted, from which the patient could not be roused in spite of massive transfusions. As it was obvious that without immediate surgery the patient would die, exploration and splenectomy were done. Death, however, occurred on the operating table.

*Kidney*.—The presence of renal injury was usually indicated by the location of the missile, which was established by x-ray examination and by the presence of gross hematuria. There were nineteen cases in which injury to the kidney was reported, and three deaths. All three patients had suffered associated severe intra-abdominal injuries involving the colon; one had also suffered rupture of the diaphragm and spinal cord injury. The combination of

Particular attention was paid to the possible development of pulmonary complications. Cough and deep breathing were encouraged, and the patients were turned frequently. Occasional bronchoscopic aspiration in the early stages of atelectasis was necessary. Intercostal block with novocain, especially in the chest cases, helped patients to raise sputum without pain. Postoperative atelectasis and pneumonia were responsible for four deaths. Injuries which immobilized the patients, such as associated fractured femur or spinal cord injury with ensuing paralysis, were major factors contributing to pulmonary complications in one-half of these cases.

*Use of Morphine.*—The abuse of morphine as a pain-relieving agent was encountered relatively often. Wounded soldiers were frequently given half-grain doses subcutaneously, as soon as they received first medical aid. A similar dose was often administered at battalion aid, collecting company, or clearing station. During this repeated procedure the patient was in shock, and the circulation was unable to pick up the subcutaneously administered morphine. Later, after adequate treatment of shock and increase in blood pressure, the accumulated morphine was suddenly absorbed and the patient developed all the signs of morphinism with its anoxia, Cheyne-Stokes respiration, etc. Oxygen and eoramine were found to be of value in such cases. In a few instances, precious hours were lost before the patient could be operated upon as a consequence of too much morphine. Intravenous administration of morphine is much to be preferred, and the drug should be given in this manner whenever possible. The administration of an overdosage of morphine should be avoided in patients already anoxic from shock, as restlessness from cerebral anoxia is thereby aggravated.

*Analysis of Deaths.*—The mortality in this series was 14 per cent. Of the fourteen deaths, six were due to irreversible shock. Two patients died on the table, and four others within forty-eight to seventy-two hours, of progressive irreversible shock. One death followed a severe bile peritonitis. Three deaths resulted from diffuse peritonitis. These patients had suffered multiple perforations of small bowel and colon. Pulmonary complications were responsible for four deaths.

TABLE III CAUSES OF DEATH IN 100 CASES

CAUSE OF DEATH	NUMBER OF DEATHS
Irreversible shock	6
Bile peritonitis	1
Diffuse peritonitis	3
Pulmonary complications	4
Total	14

*Peritonitis.*—In this entire series there was no instance of diffuse suppurative peritonitis in the true sense of the word. Among the patients examined at post-mortem, none were seen with the abdomen distended by pus, as was often the case at autopsy following intestinal perforation and operation, before the era of chemotherapy. The cases of peritonitis observed were of the fibrinoplastic type producing dense adhesions, which resulted in numerous points

the splenic flexure of the colon. In many cases, following débridement of the tract of the missile with its recovery (extraperitoneally) in the abdominal wall, laparotomy was not performed.

*Evisceration.*—Evisceration was present in eight cases; two of these patients died. In one, the defect of the abdominal wall was at least 8 by 10 cm. in size. Multiple injuries to the large and small bowel were also present. Resection of the right side of the colon and ileocolostomy was considered necessary; reconstruction of the abdominal wall was carried out over a petrolatum pack. The patient died three days later of pulmonary complications. The second soldier admitted with evisceration died of irreversible shock due to severe injuries to the colon, jejunum, and abdominal wall as well as compound fracture of the forearm, which necessitated amputation.

*Chemotherapy.*—Chemotherapy has played a significant role in the low mortality of this series and is responsible for the absence of severe peritoneal infection following abdominal injury. At completion of laparotomy it was customary to leave 100,000 units of penicillin in the peritoneal cavity, following which 40,000 units were administered every four hours intramuscularly. Intramuscular administration of penicillin was started as soon as the patient was admitted and continued as long as he remained at the field hospital. In thoraco-abdominal wounds 100,000 units of penicillin in saline solution were instilled into the chest before closure. The sulfonamide drugs were not used locally, intraperitoneally or intrapleurally. Sodium sulfadiazine intravenously, 3 Gm., was administered as soon as the patient was out of shock. Postoperatively, 6 Gm. daily were administered in the intravenous solutions. No case of renal blockage from sulfadiazine crystals was observed, although cystoscopy was performed in cases of anuria to rule out this complication. Every four hours, 1 Gm. sulfadiazine with soda was given by mouth as soon as alimentation was begun. In the course of four days this dosage was reduced to half, and subsequently discontinued, in accordance with the progress of the patient. Very few drug reactions were seen at the field hospitals.

*Postoperative Care.*—Careful attention to the details of postoperative care was considered of utmost importance. Blood volume was supported with blood and plasma, after return to the ward tent. Gastric suction was maintained for several days, until the re-establishment of normal peristalsis, as evidenced by passage of gas per rectum. Plasma was given daily in amounts of 500 to 1,000 c.c., in an effort to maintain nitrogen balance. Parenteral fluids, glucose in water and saline solution to a total of 3,500 c.c., were given during four to five days, until diet was tolerated by mouth.

If distention appeared or obstruction seemed to be developing in spite of the Wangersteen suction it was removed and replaced with a Miller-Abbott tube which in most cases was readily passed into the upper reaches of the small bowel, using mercury to weight the balloon. In only two cases did the procedure fail to decompress the bowel. One of these patients was operated upon with successful outcome, for release of adhesive obstruction, at a rear hospital to which the patient had been evacuated. The second died of peritonitis and obstruction at multiple adhesive points.

In the recent Spanish Civil War, which began in 1936, a series of 240 cases of lesions of gastrointestinal involvement alone or conjointly with other visceral wounds was reported upon. Only 25 per cent of the patients recovered.

Similar recent series from World War II, as published by Imes, Bradford and associates, and Jarvis and associates revealed an over-all mortality of approximately 20 per cent.

It is difficult to ascribe the lowering of mortality to any one specific factor—penicillin, sulfadiazine, blood, plasma, plus above all watchful postoperative treatment and alertness for possible complications. The careful treatment of shock is probably the most important single item. Adequate decompression of the bowel by gastric suction syphonage before, during, and after surgery should be mentioned as having played an important role.

Conversation with German medical personnel in captured enemy field hospitals elicited the following information: Their best mortality claim was 30 to 50 per cent. Gastric suction was not utilized by the Germans. While plasma was available, blood was not, and direct transfusions were the rule. The Germans had sulfonamide preparations comparable to ours, but no penicillin.

Much credit is due to the Medical Corps of the United States Army for its wonderful organizational and supply system, as well as to the enlisted men and nurses, who assisted in Army Field Hospitals. The excellent service rendered by the personnel responsible for the successful administration of the blood banks cannot be praised too highly.

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# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## THE IMPORTANCE OF NONSURGICAL MEASURES IN THE TREATMENT OF INTESTINAL OBSTRUCTION

GEORGE G. FISKE, M.D., BALTIMORE, MD.

**I**N SPITE of the fact that the local and systemic effects of acute intestinal obstruction have been well known for many years, the morbidity and mortality ratios in many hospitals throughout the country are still too high. This means that there are many physicians and surgeons as well, who either do not understand both the anatomy and the physiologic changes that take place in intestinal obstruction, or do not properly combine the nonsurgical forms of treatment with prompt surgical intervention. Although this paper is not concerned with the surgical aspect of the treatment of intestinal obstruction, I should like to make it clear at the outset that if a diagnosis of mechanical obstruction can be made, surgical intervention is without doubt the proper treatment. The nonsurgical measures which will be discussed here are the necessary adjuncts both before and after operation, but are not to be considered as *primary forms of treatment* in themselves.

Before we consider the various nonsurgical forms of treatment and their rationale, we should have a pretty clear picture of the disturbed physiology of both the involved intestine and the patient as a whole. When obstruction of the bowel develops from some cause, there follows a sequence of events with, first, gradual ascending distention of the bowel above the constriction, followed by alteration in the absorptive and secretory functions, impairment of circulation, and finally gangrene if the obstruction is not relieved. Vomiting usually begins early and continues with the resultant loss of fluids and electrolytes, and dehydration rapidly develops. As the blood supply of the bowel becomes impaired by distention or actual strangulation, as in volvulus or strangulated hernia, fluid passes out into the peritoneal cavity, and there is loss of plasma as well. Unless relief is afforded the process continues and the patient lapses into a state of shock followed by death. It can be seen, therefore, that if a patient is suffering from a mechanical obstruction of the small bowel caused perhaps by a cycle band of adhesions from an old operation wound, even though proper surgical measures may be indicated the patient may nevertheless die if adequate steps are not carried out to combat the loss of electrolytes, the hemorrhorrhage, and the low plasma proteins that have resulted from the obstruction. It may be helpful to summarize some of the life-saving measures that should be begun or even done immediately when a presumptive diagnosis of mechanical obstruction has been made, before operation can be considered.

As a result of vomiting and the outpouring of fluids into the peritoneal cavity, there is a danger of dehydration and shock. The first step is to replace the lost fluids and electrolytes. This is done by giving intravenous fluids. The next step is to give oral fluids. This is done by giving the patient small sips of water or weak tea. The third step is to give rectal fluids. This is done by giving the patient a rectal enema of water or weak tea. The fourth step is to give intramuscular fluids. This is done by giving the patient an intramuscular injection of a solution of sodium chloride and glucose. The fifth step is to give intravenous fluids. This is done by giving the patient an intravenous injection of a solution of sodium chloride and glucose. The sixth step is to give oral fluids. This is done by giving the patient small sips of water or weak tea. The seventh step is to give rectal fluids. This is done by giving the patient a rectal enema of water or weak tea. The eighth step is to give intramuscular fluids. This is done by giving the patient an intramuscular injection of a solution of sodium chloride and glucose. The ninth step is to give intravenous fluids. This is done by giving the patient an intravenous injection of a solution of sodium chloride and glucose. The tenth step is to give oral fluids. This is done by giving the patient small sips of water or weak tea. The eleventh step is to give rectal fluids. This is done by giving the patient a rectal enema of water or weak tea. The twelfth step is to give intramuscular fluids. This is done by giving the patient an intramuscular injection of a solution of sodium chloride and glucose. The thirteenth step is to give intravenous fluids. This is done by giving the patient an intravenous injection of a solution of sodium chloride and glucose. The fourteenth step is to give oral fluids. This is done by giving the patient small sips of water or weak tea. The fifteenth step is to give rectal fluids. This is done by giving the patient a rectal enema of water or weak tea. The sixteenth step is to give intramuscular fluids. This is done by giving the patient an intramuscular injection of a solution of sodium chloride and glucose. The seventeenth step is to give intravenous fluids. This is done by giving the patient an intravenous injection of a solution of sodium chloride and glucose. The eighteenth step is to give oral fluids. This is done by giving the patient small sips of water or weak tea. The nineteenth step is to give rectal fluids. This is done by giving the patient a rectal enema of water or weak tea. The twentieth step is to give intramuscular fluids. This is done by giving the patient an intramuscular injection of a solution of sodium chloride and glucose. The twenty-first step is to give intravenous fluids. This is done by giving the patient an intravenous injection of a solution of sodium chloride and glucose. 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The ninety-ninth step is to give rectal fluids. This is done by giving the patient a rectal enema of water or weak tea. The one hundredth step is to give intramuscular fluids. This is done by giving the patient an intramuscular injection of a solution of sodium chloride and glucose.

chlorides; second, there is a rise in the nonprotein nitrogen; third, there is an increase in the carbon dioxide content of the blood. The fall in the blood chloride was first described by MacCallum and his associates<sup>1</sup> in 1920; the rise in the nonprotein nitrogen was described by Tileston and Comfort<sup>2</sup> in 1924. The increase in the carbon dioxide content of the blood had been previously reported by McCann<sup>3</sup> in 1918. These changes are all well understood now, but it is interesting to note that in 1912, before these studies were carried out, Hartwell and Houget<sup>4</sup> made the observation that in acute intestinal obstruction, life could be prolonged by the injection of saline solution. They attributed this fact chiefly to the relief of dehydration, rather than to the introduction of chlorides. In 1927 White and Bridge<sup>5</sup> carried out some experiments on dogs in which they completely obstructed the duodenum and then studied not only the changes in blood chlorides but also the chloride content of various tissues. They came to three definite conclusions:

"1. The fall of chloride in the tissues parallels that in the blood

"2. The loss of chloride from the blood and tissues corresponds with the total amount lost through all channels of elimination. and

"3. Only the administration of both chloride and water can prevent a fatal alteration in the chemistry of the blood and tissues "

They also agreed with other investigators who have shown that neither water alone nor isotonic glucose solution is sufficient to prevent a fatal alteration in body chemistry in intestinal obstruction.

Even though these facts are incontrovertible, many times they have not been applied intelligently in the treatment of the altered electrolyte metabolism of intestinal obstruction. This has been an important reason for the continued high mortality figures in intestinal obstruction. The work of Collier and Maddock<sup>6</sup> has probably done more than anything else in recent years to call attention to the importance of electrolytes not only in cases of obstruction but also in many other conditions, before and after operation. It is still true, however, that too often fluids containing electrolytes are given in a haphazard manner. Many times 500 or 1,000 c.c. of glucose in normal salt solution or in distilled water are given to a patient as a matter of routine instead of analyzing his specific needs by careful evaluation of the clinical and laboratory data available. Therefore, in a patient with evidence of intestinal obstruction, the length of time since the onset of symptoms, the amount of vomiting, and the level of the obstruction, whether high or low, are all factors that will determine the electrolyte needs of the patient. The laboratory determinations of the blood chlorides and nonprotein nitrogen as well as the plasma proteins are also of importance and are points to be considered in determining what replacement of crystalloids will be necessary not only to get the patient into the best condition for operation, but often to save his life. It must be realized, however, as pointed out by Collier and his associates,<sup>7</sup> that there is no rule of thumb whereby it can be determined how many grams of electrolytes each individual patient may need. In the summary and conclusions of this excellent article, in pointing out the fact that sodium chloride can be toxic if given in too large quantities under certain conditions, Collier says, "It is recommended that the correction of uncompensated

extra-cellular fluid deficiency states be made upon the basis of the physiologic response to test doses of the appropriate salt solution rather than upon the basis of the plasma chloride, the  $\text{CO}_2$  combining power, the N.P.N., the plasma protein, or the hemoglobin levels."

Besides the loss of electrolytes in all cases of obstruction, there is the concomitant loss of fluids with resultant dehydration and hemoconcentration. Even though vomiting may not have been a prominent symptom, as is often the case in low obstructions, as the bowel gradually distends above the level of the obstruction there is disturbance in the secretory and absorptive mechanism. This results in the loss of large quantities of fluid in the dilated loops. Also, in cases where there is strangulation of a portion of the bowel there will be a considerable outpouring of fluid into the peritoneal cavity. As Blalock<sup>8</sup> has pointed out, the initial loss of water is usually at the expense of the interstitial fluid of the body and only secondarily from the blood plasma. The intracellular fluid is usually not affected by moderate loss of water. However, when the resorptive function of the bowel is upset and when we realize that the normal amount of gastrointestinal secretions in twenty-four hours exceeds by several times the quantity of fluid taken by mouth, it can be seen that rapid dehydration may result. It is, therefore, necessary to give parenteral fluid preoperatively, during the operation, and after operation as well. In trying to determine the amount of fluids there is no formula that can be applied. From the practical standpoint both of electrolyte and the fluid balance can be restored safely and effectively by beginning with the administration of 1,000 c.c. of 5 per cent glucose in normal saline solution and following this with 1,000 c.c. of 5 per cent glucose in distilled water. Then, depending upon the response of the pulse rate, the blood pressure, and the general condition of the patient, the decision as to further fluid and electrolyte requirements should be made.

As stated previously, in all cases of obstruction there is not only the loss of fluid and electrolytes but also plasma proteins to a greater or lesser degree. When the obstruction has been of short duration, the loss of protein is not great and its significance as far as life and death are concerned does not amount to very much. Under these circumstances the adequate replacement of water and crystalloids will prepare the patient properly for operation and will also suffice after operation until he can take protein by mouth. This will be true in most cases of obstruction that are not of long standing, or in which there is no malignant neoplasm as the primary cause of the obstruction. In the latter case, however, the loss of protein can be considerable, and although it may not have been recognized, the state of nutrition of the patient probably had been below normal for some time. There is no doubt about the fact that in many cases the deleterious effect of an existing hypoproteinemia has not been fully recognized. Ravdin<sup>9</sup> was correct when he indicated that too much emphasis, if that is possible, has been placed on the water and salt requirements of the surgical patient and too little emphasis on the mechanisms involved in keeping fluid in the blood vessels. In other words, we should be concerned about the existence of hypoproteinemia. Until recently there were only two substances that could be given intravenously that would help to restore lost protein, and these were whole blood and plasma.

With the establishment of blood banks in many hospitals, whole blood has been made readily available, and it can adequately supply the necessary protein, but repeated transfusions are necessary. Plasma as a source of protein for intravenous administration can maintain nitrogen balance as shown experimentally by Holman, Mahoney, and Whipple.<sup>10</sup> It has certain drawbacks as a source of nitrogenous nourishment, however. It would be necessary to give 500 c.c. of plasma in each twenty-four hour period in order to supply 35 Gm. of serum protein. This amount is at the low level of normal needs for an average adult but it is only the one protein, serum protein. The work, first, of Elman<sup>11</sup> and later of others, however, has shown that protein in the form of all the necessary amino acids can be given along with crystalloids in sufficient quantities to correct the condition of hypoproteinemia and a positive nitrogen balance can be created. It is now possible with amigen and other similar preparations that are available to cover not only the protein needs of the patient but even to make up deficits within a reasonable time. There is reliable evidence that glucose is necessary for the complete utilization of protein when given intravenously in the form of amino acids. Therefore, if the patient is an adult of average weight with a moderate protein deficit, to whom we give 3 L. of fluid of which 1 L. is amigen solution containing 5 per cent each of amigen and glucose, the other 2 L. being 5 per cent glucose, the patient will receive 3,000 c.c. of water, 5 Gm. of electrolyte, 150 Gm. of glucose, and 50 Gm. of protein. If further increase of electrolytes is needed, 1 or 2 L. of the 5 per cent glucose solution can be given in normal saline solution. These amounts can be given very easily by what Elman<sup>11</sup> likes to call intravenous alimentation in any twenty-four hour period, in this way the requirements of the average adult will be met for water, electrolytes, calories, and protein.

Some mention should be made at this time of vitamins. There is no doubt that vitamins have been advertised for commercial purposes far out of proportion to the real need for them. In the nonsurgical treatment of most cases of intestinal obstruction, vitamin therapy is not necessary because of the short duration of the symptoms both before and after operation. There are some patients, however, with a neoplasm of long-standing chronic infection as the primary cause of obstruction, in whom a true vitamin deficiency develops. If this is the case there are active vitamin preparations now available that can be given parenterally when needed.

It can be said without fear of contradiction that one of the most valuable adjuvants that we have at our disposal in the nonsurgical treatment of intestinal obstruction, no matter what the etiology, is the Levine tube. Its value has been appreciated for many years, but Ward<sup>12</sup> was the first to apply continuous suction to the tube in cases of intestinal obstruction. Wangensteen and Paine,<sup>13</sup> however, are responsible not only for realizing the possibilities of duodenal suction in the treatment of all forms of intestinal obstruction but also for presenting a practical method that has undoubtedly saved many lives. There is little doubt that there is a certain percentage of cases of obstruction which can be relieved permanently by duodenal suction, but it is important to remember what Wangensteen and his associates<sup>14</sup> reported: "The relative indications for

the employment of suction are so many that it would be well to reiterate a warning which has been uttered on other occasions, namely, the practice of employing suction as a test procedure to indicate whether operation will be necessary leads only to deferment of appropriate treatment. Neglect of this admonition is the most mischievous error into which one may fall in the application of suction to patients with intestinal obstruction." Too often when we have a form of treatment that at times gives dramatic results we do not realize its shortcomings as well as its advantages, and hence we feel a false sense of security. Therefore, if the duodenal tube is used early with the knowledge that it is an adjuvant in the diagnosis and treatment, and if operation is not delayed when all indications point toward its necessity, suction decompression of the stomach and upper intestinal tract will prove one of the most valuable aids that we have.

There are certain points in the proper use of a duodenal tube for suction decompression that are important. In the first place it is always wise to explain to the patient what is going to be done and the reasons for passing the tube, and also that it may be necessary to leave the tube in place for three to six days, depending upon the course of events. With the patient in high Fowler's position, the duodenal tube is passed through the nose until it reaches the stomach. It is always wise to allow the escape of as much fluid and gas as will come before suction is applied. After a short time a very moderate degree of suction is applied to discover whether there is further return of gas or of the contents of the upper intestinal tract. If the process of decompression continues it can be aided by alternately applying gentle suction and cutting it off. If, however, the stomach is emptied and there is no further recovery of fluid or gas, it is advisable to cut off the suction, place the patient on his right side, and then advance the tube about one inch every five or ten minutes. In this way it is possible in perhaps 50 per cent of the cases to get the end of the tube through the pylorus and so decompress the upper small bowel. If it is established that the tube is in the duodenum, either by the recovery of bile or by the decompression of distended loops of small bowel, it is wise to keep a moderate degree of suction on the tube.

In a majority of cases of intestinal obstruction the question arises as to how long suction drainage should be applied before surgery is resorted to. This question cannot be answered in a dogmatic way because the limitations in the diagnosis of acute abdominal disorders are too often plain to both the physician and the surgeon. However, again as Wangenstein and co-workers<sup>14</sup> have pointed out, when the significance of intestinal colic, the presence or absence of signs of peritoneal irritation, and the character of the aspirated gastric contents, together with the flat x-ray film of the abdomen are fully evaluated, it is usually possible to arrive at certain reasonably accurate conclusions. These are, first, whether obstruction is present, and, if so, at what level. Second, it may be possible to determine whether there is strangulation of bowel, and, finally, whether the obstruction is complete or incomplete. On the bases of these conclusions it should be possible to determine whether it would be safe to temporize for a while even though the exact nature of the pathologic process remains conjectural. One rule, however, can be fairly definitely laid down; namely, if col-

icky pains continue after the decompression of the stomach and there has been time for even partial restoration of the fluid and electrolyte balance, immediate surgical exploration is mandatory. The two most difficult types of cases with which we have to deal with regard to postponement of surgical intervention are those patients in whom obstruction is secondary to some inflammatory process such as a postoperative ruptured appendix, and that other often distressing group who have had more than one obstruction and, therefore, a number of laparotomies with the resultant widespread presence of adhesions. Conservatism in these two types will often be rewarded, also operation, which may become necessary, is often unsatisfactory as emphasized by Morton.<sup>15</sup>

Intestinal intubation as described by Miller and Abbott<sup>16</sup> not only has a definite place in the nonsurgical treatment of intestinal obstruction, but it is also particularly applicable to the two types of obstruction to which reference was just made, namely, that secondary to an inflammatory process and the recurrent type due to multiple abdominal adhesions. It is also true that there are a good many patients in whom gastric or even duodenal suction with the Levine tube will not afford very much relief from the distention. The principle of the Miller-Abbott tube is well known. There have been a number of modifications, but the most satisfactory is a double lumen tube with an inflatable balloon near the end. One lumen is used for the aspiration of intestinal gas and fluid while the other, which is connected with the balloon which surrounds the tube, can maintain any required degree of inflation. The tube as originally devised had what was termed a duodenal bucket on the end which had the dual purpose of assisting the tube through the pylorus and at the same time enabling its position to be located very easily under the fluoroscope. Other innovations have been used in its place, such as putting mercury in the balloon or attaching a small number of buckshot tied in a bag at the end of the tube, the purpose being to facilitate the passage of the tube through the pylorus. When the tube has once passed into the duodenum and the balloon has been partially inflated, there is no doubt that the tube will advance and decompress the bowel in the presence of either mechanical obstruction or adynamic ileus.

Encouraging results have been reported by Abbott and Johnston<sup>17</sup> and others with the use of intestinal intubation, but the method has definite limitations as well as many difficulties connected with its use. In the first place, it is a time-consuming measure even in the most experienced hands. It is frequently necessary to watch the course of the tube by fluoroscopy, which means constant handling of a patient whose general condition may be definitely precarious. The most serious drawback to this method in the hands of many physicians is the difficulty in getting, and indeed in many cases the failure to get, the end of the tube through the pylorus in any reasonable time. It is one of those procedures that should not be relied upon by the surgeon who has treated only occasionally a case of obstruction, but should be used in a properly selected group of cases by the surgeon who has had the opportunity and the patience to work with the method frequently and to devise his own maneuvers that will make the difference between success and failure. There are many procedures that have been described by various surgeons that are of great value in their

own hands because they understand their intricacies and know how to use them. In other hands, however, whether experienced or not, a particular procedure may not yield the same good results, a fact which is due to the personal equation that too often is not given the proper consideration. I feel that the use of the Miller-Abbott tube is in this category. If it is used in the proper group of cases by experienced hands it will prove a tremendous asset; if valuable time is wasted in attempting its use by those who are not familiar with it, the mortality rate will rise as a result. It should be added in justice to those who have developed this method that they have not advocated its use in the treatment of obstructions of the large bowel or if there is any indication of strangulation of the bowel. It is obvious that in the presence of strangulated hernia, temporization instead of operation may bring about disastrous results.

Up to the present point, the discussion has outlined the nonsurgical treatment of intestinal obstruction with due regard to the fact that operation for complete relief will be necessary in the great majority of cases. Naturally, if the patient responds to conservative measures and shows real improvement as contrasted with the false security that may be engendered in the surgeon following partial abdominal decompression and replacement of fluids and electrolytes, although the obstruction has not been relieved, operation may be safely deferred. When laparotomy is necessary the two measures already begun, which should be continued during the surgical operation, are the parenteral administration of fluids and siphon drainage of the stomach and upper intestinal tract. Drainage can be accomplished by letting the distal end of the duodenal tube, which has already been inserted, hang down over the edge of the operating table as low as it will and at the same time having it unclamped. This plan will allow the escape periodically during the operation of fluid or gas that may be forced upward by any necessary handling of the bowel. Often the nasal tube is clamped off during the period of the operation and this not only is not helpful to the surgeon but also may be definitely harmful to the patient.

There are certain measures that are necessary during the postoperative period to ensure the complete relief which both the patient and the surgeon desire. In the first place, gentle suction applied to the duodenal tube should be started again as soon as the patient has been returned to the bed. It is not possible to state any definite time during which suction should be continued, but in most cases it is well not to stop it until the patient has had at least one or two voluntary stools and the abdominal distention has definitely subsided. When this point has been reached it is wise to stop the suction and then clamp off the tube for periods of about two hours while at the same time the patient continues to take some fluid by mouth. If after this procedure has been repeated a number of times there is not much return of fluid from the tube when suction is reapplied, as a rule it is safe to remove the tube. It is usually at this time that the patient once again feels that he is really going to get well, and the surgeon feels considerable relief also. At times it is necessary to leave the duodenal tube in place for as long as a total of six to eight days, this can be done with surprisingly little discomfort to the patient when the tube is fixed with

adhesive tape at the point just below where it emerges from the nose in such a way that the tube cannot move in or out and so cause irritation

The parenteral administration of adequate amounts of water, crystalloids, and protein in the proper proportion is, if possible, even more important after operation than it was before. In order to accomplish this it is necessary to correlate certain known daily requirements of the body with the total loss of fluids and waste products in any twenty-four hour period. In other words, it is necessary to keep an accurate account of the total fluid intake parenterally and orally, and also the total fluid output including drainage from the duodenal tube, urine excretion, and vomitus, if any. In this way it is possible to determine accurately whether the positive fluid balance which is so essential to the normal convalescence of the patient is maintained.

It has been shown experimentally and noted clinically by numerous observers that there is always a definite degree of adynamic ileus accompanying any mechanical obstruction. The degree of paralysis of the bowel is usually in direct proportion to the length of time that the obstruction has been present. When there is added the trauma incident to surgical operation for relief of the obstruction, even though this may be kept to a minimum, the problem with which we are faced after operation is to afford the patient relief from adynamic ileus. As has been mentioned, perhaps the most important step in accomplishing this result is to establish and maintain a positive fluid balance and also to add the proper amount of crystalloids and proteins parenterally until the patient is able to take the necessary requirements by mouth. As stated previously, if the average patient is given in a twenty-four hour period a minimum of 3,000 cc of water, 5 Gm. of electrolyte, 150 Gm of glucose, and 50 Gm of protein, he should remain in the proper balance. There should be, however, a minimum output of 1,200 cc of urine in each twenty four hour period. If it is necessary to give additional fluid to maintain this output it is best to give it in the form of 5 per cent glucose in distilled water. This supplies extra nourishment as well as increases the urinary output. There is no reason why water should not be given to the patient by mouth by starting with small amounts very soon after operation, because with the suction maintained by the duodenal tube there is no danger of an accumulation in the stomach or upper intestinal tract. The patient obtains definite benefit from drinking water even if it is mostly of a psychic nature at first.

The role of drugs in the treatment of intestinal obstruction is not an important one, and there is considerable difference of opinion as to both their methods of action and their effectiveness. During the preoperative period drugs have very little place. Too often morphine is given when the possibility of intestinal obstruction is not suspected and the signs and symptoms are masked so that the true diagnosis is not made early and the institution of adequate treatment is delayed. Postoperatively, morphine has a definite place. As shown conclusively by Puestow,<sup>15</sup> morphine in moderate doses increases peristalsis in the small intestine but at the same time decreases it in the colon. However, he and others have shown that pitressin will stimulate peristalsis in the colon, and there is no doubt from clinical evidence that if a rectal tube is inserted just be-



fore an ampule of pitressin is given intramuscularly most patients with distention of the colon will respond very well. The only other drug that various investigators have reported as having any uniformly stimulating effect on the peristaltic action of the small bowel is prostigmine. A regimen which has proved satisfactory after operation in most cases of intestinal obstruction as far as the use of drugs is concerned, is to give morphine, usually  $\frac{1}{8}$  gr. but never more than  $\frac{1}{6}$  gr., as often as every four hours if necessary to give the patient reasonable comfort. At the same time, starting usually four hours after the patient has returned to the ward, 1 c.c. of pitressin may be given every four hours alternating with prostigmine, 1 c.c., every four hours. This means that for the first twenty-four hour period after operation the patient will receive pitressin and prostigmine alternately at two-hour intervals.

There are some surgeons who do not feel that enemas are of benefit in the treatment of intestinal obstruction. In 1936 Ochsner<sup>29</sup> stated categorically, "Enemas, flushes and cathartics have no place in postoperative treatment." For the rationale of this statement he pointed to the fact that in ileus the bowel is already distended and the musculature is functionally inactive, therefore, the patient will not be able to evacuate the fluid of the enema any more than he could his own gas and fluid. This will undoubtedly prove to be the case if large quantities of fluid are given or if an attempt is made to flush out the colon. If, however, a water and glycerin enema of not more than 250 c.c. is given not oftener than twice in each twenty-four hour period and is given just before the pitressin is due, excellent results will obtain in most cases. As Puestow<sup>30</sup> said, "Pituitrin or pitressin combined with enemas serves very well to relieve the distress by emptying the large bowel." After the patient has had a number of effectual enemas, their further employment depends entirely upon the clinical progress.

There are two other adjuvants in the postoperative treatment of intestinal obstruction that should be mentioned because there are times when they prove of definite benefit. The inhalation of 95 per cent oxygen as employed by Fine and others<sup>31</sup> has a sound theoretical basis, and when it is administered with a Boothby apparatus it can be done effectively and very economically. There are, however, many patients who do not respond, at least to this therapy alone, and it can be considered only as one more means which may be tried to help relieve distention. The other form of treatment that undoubtedly makes the patient feel more comfortable, although it is doubtful how much actual benefit he derives from it, is the application of heat to the abdomen. Hot stupes and dry heat have been advocated by physicians and surgeons for the relief of abdominal distention for many years, but it is questionable how much actual benefit has ever been derived therefrom.

#### SUMMARY AND CONCLUSIONS

It has been well stated by Veal<sup>32</sup> that "the mortality rate of acute intestinal obstruction is largely the mortality of delay and rises each hour that proper treatment is delayed." Because of the difficulty, first, in establishing a definite diagnosis of obstruction in many cases, and, second, of trying to determine how

far conservative treatment can be followed before operation is imperative, the task of carrying out "proper" treatment is not always an easy one. Certain essentials, however, can be enumerated as follows:

1. Restore lost fluids, crystalloids, and protein by parenteral administration without delay.
2. Be guided as to amounts that should be given by the clinical picture of the patient as well as the use of laboratory tests.
3. Establish suction drainage of the stomach and upper intestinal tract by means of a nasal tube immediately after the diagnosis of intestinal obstruction has been made.
4. Do not delay operation, particularly when cramplike pains persist after decompression of the stomach and upper intestinal tract.
5. Continue postoperatively the parenteral administration of proper amounts of fluid, crystalloids, and protein when necessary, until adequate amounts can be taken by mouth.
6. Continue suction drainage of the stomach until the bowels have moved and distention is relieved.
7. Use judiciously morphine, pitressin, and prostigmine together with small water and glycerine enemas; this is helpful in combating postoperative ileus.
8. It has been shown by the excellent reports of Veal<sup>21</sup> and of Moses<sup>22</sup> that the mortality rate of intestinal obstruction can be reduced to a low figure in obstructions of the small bowel by the proper combination of nonsurgical treatment with good surgical care. Comparable results can be obtained in obstructions of the large bowel as well.

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## Book Reviews

**Nursing in Commerce and Industry.** By *Patricia J. Motterath, R.N.*, New York, N.Y. 1956. New York, 1956, 110 pp., \$4.00 (Harcourt, Brace & Co.).

In preparing this volume Mrs. Motterath and the National Organization for Public Health Nursing have recognized the fact that although over 13,000 nurses were employed in this type of work during 1953 no book existed which attempted to delineate the scope of the industrial nursing program. The problem is to be encountered in the future as the industrial field of these nurses has rapidly expanded since no separate medical field of assignment and most of them have been employed in programs that were lacking medical direction. It is for a number of years such organizations that the industrial nursing programs have varied widely in the number and quality and that the future programs will be a fine point in time to follow the expansion of the latter area.

This book represents an attempt to bring together the experiences of many nurses and physicians in the industrial nursing field. After several introductory chapters on the plan of the book in the industrial organization, attention is given to various types of problems that may be encountered. Several of the chapters are written by physicians.

It is noticeable that the reader will find much to read in a book of this character for it represents a program as well as a field where a knowledge of specific areas are great. Mrs. Motterath is indebted to Mrs. Motterath's long experience that industrial nursing is a field which has grown to extend far from a field of nursing rather than a specialty of public health nursing in the industrial setting and experience in the latter field. This program has resulted in the form of much material that would have been learned in the usual job of industrial nursing nurse. Some of the chapters on the role of the nurse in industrial nursing are written by the program that is found in the field as well as a different rather than a situation in the management of the industrial setting in industry. Others will take exception to her concept of a nurse's role's program in the management and part of the program in the industrial field of the other major departments of the industry.

Each chapter is written by an author and is written in a book which deals with a specific industrial nursing and it is written in a field character and by a physician and a nurse. Mrs. Motterath has attempted to present these chapters although clearly expressing her own ideas. The reader will find the book of nursing and public health and the nursing field of information. In writing this the information is written in a field which is written in the same who writes the field without experience in writing in public health. The writing is written and published with frequent errors although it is written. In many parts the book could be considered as a book which is written by parts were somewhat different.

As a result of a review of the character and character part. They should not always state that the book is a very good one that it is packed with useful information to be found in a review and that it is a valuable book interest and discussion of an important field of industrial nursing and health care.

**Acute Injuries of the Head, Their Diagnosis, Treatment, Complications and Sequels.** By *H. P. Pouchot, M.D.*, Surgeon in Charge, Department of Neurological Surgery, New York Hospital Hospital, New York, N.Y. 1956. Pp. 424, with 204 illustrations. Dutton Press, 1956, 110 pp., \$4.00 (Harcourt, Brace & Co.).

This book was written primarily for those physicians who are responsible for the treatment of acute cerebral trauma and not who have not received special training in neurology and neurosurgery. It is an effort to present a continuous picture of the problems arising

during the care of a patient with a head injury and an attempt to outline the treatment. Mr. Rowbotham is well qualified to edit this book because of his extensive experience both before and during the recent war. In this second edition, he has rewritten many chapters and has included experiences of British neurosurgeons in World War II. Throughout the book is stressed the fact that for good results and early readjustment following a head injury, a patient must have continuous and coordinated treatment beginning at the time of injury and continuing until he is resettled in employment.

The first section of the book concerns the mechanism of head injuries and includes a discussion of fracture patterns as well as the work of Dr. Holbourn of Oxford on the theory of injury to the brain by the forces of rotation. The section on pathology presents clinical rather than histologic studies of concussion, cerebral herniation, hematomas and hygromas, the development of the neurologic picture, and the cause of death in head injuries. In the section on diagnosis, signs diagnostic of the different types of head injury, special tests used, and graphs illustrating typical clinical stages of regression and of recovery are presented. Special signs such as delayed decerebrate rigidity, fixed dilated pupils, and prolonged unconsciousness are given as indications of poor prognosis. The section on closed injuries and on compound wounds is well written. The techniques advocated are standard, however, only briefly mentioned is the use of fibrin foam for hemostasis and of tantalum for cranioplasties. An adequate summary of the treatment of osteomyelitis of the skull is given. The highlight of the book is the section on the results of injury to special parts of the brain and skull. Injuries of the neural optic system are well discussed. The basic causes of the sequelae of head injuries, both organic and inorganic, are well evaluated. There is a chapter on rehabilitation in which the center at the Castle of Callaly is intimately described. The book ends with a chapter on the mechanism of birth injuries.

Important to students of head injuries is a well indexed and extensive bibliography of the English, French, and German literature.

The book has the disadvantage of being written by one man with all the opinions and interpretations based on his experience, however, it is an invaluable contribution to a higher standard of treatment of head injuries.

**Medicine in Industry.** By Bernhard J. Stern, Ph.D., Lecturer in Sociology, Columbia University. Pp. 209. New York, 1946, Commonwealth Fund. \$1.50.

There has long been need for a compact discussion of the community health problem occasioned by industrial employment and for an objective description of the various measures that have been tried to solve these problems. In this book Dr. Stern, who is sociologist maintaining teaching connection in both Columbia and Yale Universities, has provided such a volume. After a brief discussion of the awakening of our consciousness of the problem of industrial health, and somewhat longer consideration of the social and legislative background of modern industrial medicine, Dr. Stern presents a careful analysis of the present problems of industrial disability and the handicapped worker. He analyzes the preventive services now available, the successes and failures of health insurance plans, and the place of the industrial physician. He concludes that none of the methods now applied to American industry has been adequate to meet the needs for better prevention of hazards and comprehensive medical service within the financial capacity of the worker. Dr. Stern does not attempt to plead the case of any specific reform. The book represents merely a critical and highly objective appraisal of present problems. In preparing this volume for the series of monographs sponsored by the New York Academy of Medicine, Committee on Medicine and the Changing Order, Dr. Stern has produced the best available appraisal of the current status of the industrial hygiene movement. The book should be read carefully by all who are interested in this expanding field or who are concerned with the general problem of the changing patterns of medical practice.



# SURGERY

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## Original Communications

### PRIMARY ANASTOMOSIS IN THE TREATMENT OF CARCINOMA OF THE COLON

RAYMOND W. MCNEALY, M.D., CHICAGO, ILL., AND  
VICTOR G. LANDS, M.D., BEVERLY HILLS, CALIF.

**I**N THIS paper we present a series of thirty-four consecutive cases of open anastomosis in various parts of the large bowel. There was no mortality directly attributable to surgery. There were two deaths in the thirty-four cases. The first occurred in a 62-year-old woman patient on the seventeenth postoperative day, following a segmental resection with primary anastomosis for cancer of the sigmoid. The patient was to have been discharged from the hospital the following day, but died suddenly of a pulmonary embolism. The second occurred in a 58-year-old woman on the sixth postoperative day following a primary resection of the sigmoid for cancer. This patient died of a coronary thrombosis. These anastomoses were performed over a period of twenty-seven months (September, 1943, to January, 1946). In none was a complementary cecostomy used; all patients received the routine preparations outlined in this paper. Seven of the patients had obstruction or partial obstruction on entrance to the hospital, but were relieved of their obstruction (as outlined below), so that a primary anastomosis could be performed at a later date with safety. No patient developed a fecal fistula and no patient developed obstruction after operation.

The changing history of bowel resections is fascinating, if only to note how the recent application of modern biochemical and physiologic principles has helped us approach more ideal surgery with less trepidation than in the past.

The earliest bowel resections were completed with primary anastomosis. Most of these attempts, however, were discouraging.

The first successful resection with primary anastomosis was performed in 1833 by Reybard on a 28-year-old man who had carcinoma of the sigmoid. In 1843 Thiersch resected an acutely obstructed colon. By 1880 ten resections had been recorded, three of which were successful. In 1881 Kocher reported a successful resection with end-to-end anastomosis. By 1881 Billroth had reported

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seventeen cases with ten deaths, a mortality of about 60 per cent. By 1889 his clinic had reported fifty-seven cases with nineteen deaths, a mortality of 37 per cent.

More than 60 per cent of the operative deaths were due to peritonitis. The era of resection with primary end-to-end anastomosis was fast coming to a temporary interruption. In its place surgeons were encouraged to use the multiple stage operations of which the so-called Mikulicz operation is best known. The only well-supported claim for its popularity was found in the reduced mortality over that of the single stage resection with primary anastomosis.

In reporting sixteen cases with two deaths, a mortality of 12.5 per cent, Mikulicz lowered considerably the best previously reported mortality, namely, 37 per cent.<sup>22</sup> However, this procedure never attained universal acceptance because of certain undesirable features: From the standpoint of the patient—the uncomfortable flow of feces over an excoriated skin, the multiplicity of operations, the time consumed, and the expense of several hospital stays. From the standpoint of the surgeon—the limitations on the amount of mesentery which may be excised without impairing the blood supply (such impairment leading to necrosis, leakage into the peritoneal cavity, and death), the danger of implantation of cancer cells in the abdominal wound because not enough of the carcinomatous mesentery can be excised safely, and the impossibility of exteriorizing bowel with a short, fat mesentery.

In spite of the progressive ascendance of the use of the exteriorization procedure, there were always a few intrepid, visionary surgeons who attempted and hoped to achieve successfully the ideal primary anastomosis.<sup>7, 11, 16, 17, 18, 23</sup> And if they failed, it was not always because their technique was inadequate or contaminating. They failed many times because they did not recognize certain fundamental principles of colon physiology and pathology.

Practically every cancer of the colon, especially the left colon, is partially obstructive. Multiple enemas and continuous intestinal decompression by suction had not yet come into vogue. Had the surgeon a better knowledge of these valuable adjuncts (so that the colon could be emptied adequately before surgery, permitting the distended, hypertrophied, and edematous intestinal wall to regain its normal tone and size), primary anastomosis would have been the procedure of choice in resectable, nonobstructive carcinoma of the colon. No technique, open or closed, will give a high rate of successful primary anastomosis if the sutures have to be taken through soft, boggy tissues and in the presence of infection. Yet that is what the pioneer surgeons attempted. No wonder they had a high mortality. More wonder their success, as small as it was. With this ideal of primary anastomosis in mind it was no surprise that surgeons attempted to devise instruments and methods<sup>19, 24</sup> which would theoretically prevent contamination of the suture line and peritoneal cavity. In 1891 Halsted<sup>13</sup> attempted to develop a relatively aseptic method. He emphasized the fact that the submucous layer of the gut wall was the true layer of strength; hence, all that was necessary was to perforate the submucous layer without penetrating the mucosa. This was, and is, a theoretical not a practical solution. Moreover, it was due more to a late leak at the suture

line and less to a contamination at operation which led to the terrible incidence of peritonitis. This fact seems to have escaped early workers.

About this time other surgeons attempted closed anastomosis by clamping the ends of the two limbs of bowel and performing an anastomosis over the clamps. The diaphragm between the two limbs was then broken with the fingers after the clamps were removed. In 1908 Parker and Kerr<sup>26</sup> used a so-called basting stitch to close the ends of the bowel, made their closed anastomosis, and then removed the basting stitch. Again the diaphragm had to be broken down by finger manipulation. Both Horsley and Stone have had obstructions with this method.<sup>4</sup> Other men have been enthusiastic over closed methods of anastomosis (Schoemaker,<sup>21, 22</sup> Halsted,<sup>14</sup> Fraser and Dott,<sup>19</sup> Furniss<sup>11</sup>). However, obstructions have been reported with methods of Halsted and Fraser and Dott due to projection of tissue into the lumen at the line of anastomosis.<sup>4</sup> Senn pointed out that "If . . . more than a few lines of the margin of the bowel is inverted between the two rows of sutures, there is great danger of causing primary traumatic stenosis of the projecting circular ring in the lumen of the bowel."

In recent years Rankin,<sup>23</sup> Gibbon and Hodge,<sup>12</sup> Owings and Stone,<sup>23</sup> Stone and McLanahan,<sup>23</sup> Wangenstein,<sup>27</sup> and others have been ardent exponents of the closed method. Yet Charles W. Mayo was able to report a mortality of 8.4 per cent with eighty-three cases of carcinoma of the right colon, counting deaths from all causes regardless of the time spent in the hospital.<sup>18</sup> Open, one-stage anastomosis was used in these cases. In 1931 Cheever<sup>8</sup> reported a series of interesting cases, using an open method of anastomosis. He achieved the low mortality of 8.5 per cent when a complementary eccectomy or colostomy was used. Without a complementary vent his mortality went up to 24 per cent. However, with the use of continuous suction such complementary vents are not only unnecessary, but are in fact a burden because of potentially infected wounds, further operations, etc.

Some twelve years later Whipple was able to point out "that with the proximal bowel decompressed (by use of Miller-Abbott tube and suction), the hazard of spillage and contamination is eliminated and the anastomosis by the open method, with careful protection of the wound and remaining peritoneum and accurate suture technique, is as safe as the so-called aseptic methods, and more certain of giving an adequate stoma and avoiding subsequent leakage."<sup>35</sup>

It can hardly be denied that it is much better to work with freshly cut edges (not crushed ends) under direct visual inspection and see each stitch accurately placed than to suture crushed edges with sutures that cannot be visualized completely. We have no special prejudice against mechanical gadgets as such, but where these become a possible blind for fundamental principles, we advise caution.

*Preoperative Preparation of the Colon.*—The principles of preoperative care involve thorough cleansing of the bowel; fortification of the liver with respect to glycogen storage; correction of dehydration, anemia, protein, and vitamin deficiencies; general restorative measures; sulfonamide prophylaxis; the use



of suction when properly indicated; *fluoroscopic examination in all bowel cases to eliminate any possibility of the presence of retained barium.*

On admission the patient with carcinoma of the colon falls into one of two classes: (1) Obstructive or partially obstructive; (2) nonobstructive. The treatment of these types varies accordingly.

#### OBSTRUCTIVE CASES

The extent of the pathology in the colon in the obstructive phase determines operability. During the final stages of an obstruction due to carcinoma of the colon, when a partial obstruction becomes complete, the proximal colon becomes distended and there is encroachment upon the blood supply, with devitalization of the mucosa and consequent ulceration. The highly virulent bacteria seep through the soggy, edematous wall, so that the patient becomes toxic and has a low-grade fever. If the patient gets no relief, perforation may occur. A patient with such an obstruction presents all the physiologic and anatomic problems of an individual with a margin of safety so narrow that he must have the benefits of well-planned pre- and postoperative attention if he is to survive. The patient has usually had a restricted diet and is vomiting, dehydrated, and anemic.

The management of the obstructive phase requires careful observation and the use of ingenious nonoperative methods for relieving the obstruction. The patient is typed and cross-matched and receives immediate intravenous fluids. A Levine duodenal tube is inserted intranasally and continuous suction started immediately. A cleansing enema is given, and one hour later the patient receives one ounce of mineral oil by mouth. When the oil is given, the suction is stopped for twenty minutes. The enemas and mineral oil are administered on alternate hours until the oil comes through in the enema washings or until the patient is passing gas and feces freely by rectum.

The purpose of this regime is to convert a complete or partial obstruction into a nonobstructive lesion. When a carcinomatous lesion produces obstruction, it is mainly the secondary features of the carcinoma (with all that this implies, such as inflammation, impaired circulation, and edema in and about the lesion) which obstruct the lumen. Not infrequently a bit of inspissated feces or barium (administered either by mouth or by rectum) plugs the narrow lumen and, together with the increasing inflammation and edema, produces a complete obstruction.

Feces are usually liquid in the right colon and more dehydrated in the left; hence, the lower-lying lesions are the ones which obstruct early.<sup>30</sup> If one is able to dislodge the feces or barium by large enemas from below and relieve the forward pressure by suction from above, then there is a better chance for the secondary edema to subside. The lumen in the region of the lesion will enlarge and gas and feces will pass.

Once such a patient shows signs of increased peristaltic sounds and passage of gas and feces and oil from below, suction is stopped and the patient is put on a course of succinylsulfathiazole. A liquid, nonresidue diet is given for a few days and is then changed to a high protein, high carbohydrate, low

fat, low residue diet. A soap-suds enema is given twice daily. The day before surgery an enema is given every two hours or until the returns are clear. The colon must be thoroughly cleansed with repeated enemas and all residual barium washed out (as shown by preoperative fluoroscopy). Food is stopped twenty-four hours before surgery, but the succinylsulfathiazole is continued.

Any attempt to do a successful end-to-end anastomosis must assume that the patient has been brought back to near physiologic normal, both locally and systemically. The colon must be empty and it must possess normal tone and normal healing powers.

#### NONOBSTRUCTIVE CASES

Nonobstructive cases offer no serious problem of preoperative preparation. The patient is given a purge, usually one ounce of magnesium sulfate; large, cleansing enemas twice daily; succinylsulfathiazole is administered by mouth, together with a high protein, high carbohydrate, low residue diet. The plasma, hemoglobin, and vitamin levels are checked and brought up to par. At the end of about one week the patient is usually ready for surgery.

**Preoperative Preparation.**—The entire late history of the problem of primary anastomosis revolves intimately about the newer concepts of adequate pre- and postoperative management.

**Sulfonamide Prophylaxis.**—One of the causes for poor end results in large bowel surgery, especially in primary anastomosis, has been peritonitis due to late leaks through the suture line and bacterial contamination of the peritoneal cavity. Ever since Moore and Miller (in 1942) synthesized and Poth<sup>21</sup> demonstrated the intestinal antiseptic action of succinylsulfathiazole, there has been strong hope that primary anastomosis of the bowel would become a much safer procedure. Succinylsulfathiazole approaches the ideal antiseptic because it is poorly absorbed from the alimentary canal and has strong bacteriostatic properties. Even though it does not sterilize the feces, it helps bring about a marked reduction in the *Escherichia coli* and anaerobic bacilli stool count. After one week of administration, according to Poth, the *Esch. coli* count drops from an average of 10 million to less than 1,000 organisms per gram of wet stool. Since succinylsulfathiazole is so poorly absorbed from the intestinal tract (blood levels vary between 1 and 2.5 mg. per cent), it has a low antibacterial action in the peritoneal fluids.

Succinylsulfathiazole has additional virtues perhaps not considered in its original use. It so alters the bacterial flora that the consistency of the stool after one to seven days of therapy becomes "semi-fluid, small in bulk, somewhat gelatinous in appearance, and relatively odorless." The bowel becomes free of gross fecal material and gas. In addition, succinylsulfathiazole is relatively nontoxic.

The colon bacilli reappear rapidly in the feces on withdrawal of succinylsulfathiazole. Hence, the oral administration of the drug is begun as soon as possible postoperatively. This in itself produces little or no vomiting and the readministration of the drug may start within the first twenty-four hours postoperatively. The period required for achieving maximum reduction in

TABLE I. ORDERS FOR NONOBSTRUCTIVE BOWEL CASES

## PREOPERATIVE PROCEDURE

## Work up

1. Complete blood count
2. Urinalysis
3. Wassermann and Kahn
4. Blood ceritamic acid
5. X rays (as directed by surgeon)
6. Type patient and obtain compatible donors
7. Stool to laboratory
8. Weigh patient
9. Special tests as indicated:
  - (a) Total blood protein
  - (b) A/G ratio

## Medication

1. Succinylsulfathiazole
  - (a) 0.25 Gm. per kilogram body weight per 24 hours
  - (b) 0.25 Gm. given as one dose Stat., then  $\frac{1}{6}$  of that amount given every 4 hours thereafter for 5 days before surgery
  - (c) In instances where the patient cannot tolerate such a large initial dose, the drug can be administered more gradually, i.e., 3 Gm. every 4 hours for 7 to 14 days preoperatively
2. Ceritamic acid, 1,000 mg. in divided doses
3. B<sub>12</sub> vitamin capsules, 1 t i d
4. Fluids, 3,000 c.c. daily (q v)
5. Blood transfusion, plasma, or amino acids
6. Mineral oil, 1 oz q nightly
7. Urotropin, gr. 7½, t i d, for 5 days
- Sodium acid phosphate, gr. 10, before surgery
8. Antiseptic mouthwashes
9. Night medication
10. Morphine sulfate, gr.  $\frac{3}{4}$
- Scopolamine, gr.  $\frac{1}{120}$ , 1 hour before surgery

## Management

1. B<sub>12</sub> carbohydrate diet (nonresidue)
2. Dextin sweetened fluids and fruit juices between meals
3. Normal saline enemas, 2 to 4 times daily
  - (a) Saline solution enema once or twice daily for 3 days before surgery and every 2 hours on the day before surgery until returns are clear
  - (b) If the lesion can be visualized through a proctoscope the bowel may be cleansed further by irrigating through a catheter inserted beyond the lesion

## POSTOPERATIVE PROCEDURE

## Work up

1. Record fluid intake and output
2. Complete blood count
3. Urinalysis

} as ordered

## Medication

1. Morphine sulfate, gr.  $\frac{1}{6}$ , for pain or restlessness
2. Antiseptic mouthwashes
3. Fluids, 3,000 c.c. per 24 hours
4. Sodium sulfadiazine in distilled water, 5 Gm. daily for 2 or 3 days postoperatively
5. Penicillin (as ordered by surgeon)

## Management

1. Nothing by mouth until ordered.
2. Catheterization q 12 to 15 hours or for distress (instill 5% argyrol after catheterization)
3. Blood transfusion as indicated
4. Oxygen (if necessary)

colon bacteria is from five to seven days. The drop for *Clostridium welchii* and *Streptococcus fecalis* rather closely parallels the drop in the number of colon bacilli except that it takes a little longer—six to eight days. We have been using the following dosage of the drug: 0.25 Gm. per kilogram body

weight per twenty-four hours given as one large dose stat., and one-sixth of the original dose given every four hours. The same dose has been used post-operatively.

We must realize, however, that sulfonamide prophylaxis and therapy must not alter good judgment in the selection of cases, nor make for poor surgical technique, nor fail to take cognizance of other important pre- and postoperative measures.

*Protein and Hemoglobin Levels.*—Any patient who has a well-marked anemia should be regarded as a questionable risk for surgery. We are thoroughly familiar with the diminished oxygen-carrying power of hemochromic and cytopenic anemias, but we are probably not as conscious of hypoproteinemias and tissue protein deficiencies as their importance would warrant. The term *protein deficiency* is more appropriate than *hypoproteinemia* because the latter is a description of the circulating proteins which merely mirror the total protein depots of the body. When there is sufficient depletion of tissue proteins, then the circulating proteins manifest themselves as a hypoproteinemia (the ratio of tissue to circulating proteins is considered to be 30:1).<sup>21</sup>

The hypoproteinemic patient may develop generalized edema, including edema of the viscera, brain, and gastrointestinal tract. Edema of the colon may lead to subsequent obstruction of the new stoma (in cases of primary anastomosis) with nausea and vomiting and possible rupture of the suture line. Edema of the kidney may lead to a nephrotic syndrome with oliguria or anuria. Furthermore, hypoproteinemia produces a deficient tissue collagenic reaction with unpaired wound healing. Of all major surgery, carcinoma of the colon, bowel obstruction, and generalized peritonitis produce the largest decrease in plasma proteins.<sup>22</sup>

These findings suggest that a very determined effort should be made to correct protein deficiencies in all patients who undergo major surgery, especially patients with carcinoma of the bowel. Correct use of plasma, whole blood (which produces a greater rise in protein levels than does plasma), amino acids, dextrose, and saline solutions must depend on frequent observations of the patient's total plasma protein levels, hematocrit readings, and hemoglobin estimations. We should like to stress the point that in patients with protein deficiencies, transfusions of less than 2,000 c.c. rarely bring the total plasma protein levels up to minimal requirements. The slow response in plasma protein levels implies extensive tissue protein depletion which must be satisfied before plasma protein levels offer an accurate index.

Hence, it has been our policy for some time to take total protein and albumin globulin ratio levels on all patients undergoing major surgery, especially those who may have had long-standing dietary unbalances with reference to protein and vitamin intake. These patients have starved themselves either voluntarily because of a sitophobia or because the prescribed diet to relieve the gastrointestinal distress had been insufficient. The patient with a low total protein or a reversed albumin-globulin ratio is a poor risk from the standpoint of postoperative management.

*Vitamin Therapy.*—Wound healing and the reparative processes which accompany intestinal anastomosis are a function of the tissue depots of the body as reflected by the plasma protein of the blood; however, they also depend on the efficient levels of other factors. It is of little avail to saturate a surgical patient with proteins if the lack of these other factors is not adjusted. It has been demonstrated repeatedly that low vitamin C levels manifest themselves histologically by the lack of collagen which is a basic substance of tissue repair. With this defect in collagen production the whole architecture of the healing wound is disturbed.<sup>15</sup> It has been our practice to determine vitamin C levels as soon as the patient is admitted. When subnormal levels are found, we begin large doses of vitamin C intravenously: 1,000 mg. of vitamin C are given daily, preferably in divided doses in the preoperative intravenous glucose or salt solutions. These are supplied by the slow drop method. This type of management is predicated on the fact that there is a very low renal threshold for vitamin C. Its rapid elimination from the blood may be minimized and the effective rate of tissue absorption increased by prolonging the period of administration. The ability of the tissues to absorb and store vitamin C is limited as to rate, and tissue saturation even with very large doses cannot be attained before five to seven days. However, the most acute need for collagen efficiency occurs when the sutures which have been inserted begin to cut through and lose their supportive strength. This period is somewhere between the third and seventh postoperative days. Thus, in a patient with a very low vitamin C level, tissue saturation could be attained at the time of greatest need if the patient were placed on a high vitamin C regime immediately on the decision to operate or upon admission to the hospital.

Prothrombin levels are checked preoperatively and adjusted accordingly either with synthetic vitamin K substances or with liberal fresh whole blood transfusions. We use routinely 5 to 10 mg. of vitamin K daily in the preoperative intravenous fluids.

Vitamin B complex deficiencies manifest themselves in vicious cycles in which absorption and utilization from the gastrointestinal tract become progressively impaired. A surgical patient has an increased need for the vitamin B complex due to the parenteral use of glucose and saline solutions. The oxidation of carbohydrates utilizes the B coenzyme factors, and the increased diuresis carries with it water-soluble B vitamins. Impaired preoperative absorption and postoperative dietary restrictions lead further to depletion of the B complex stores. We attempt to re-establish and maintain tissue saturation of the B complex by daily administration in the pre- and postoperative intravenous fluids.

*Postoperative Management.*—The gastrointestinal tract is kept at rest as long as possible postoperatively. The patient is usually given a transfusion on the first or second postoperative day. The plasma and vitamin levels are maintained and the fluid balance controlled. The Levine tube is kept in place during surgery and postoperatively until the patient begins to pass gas and feces freely per rectum. Before the patient is removed from the operating table, the sphincter control of the anus is temporarily paralyzed by dilatation.



The rubber-covered clamps are brought side-to-side, mesenteric edge to mesenteric edge. One suture is now inserted at the mesenteric attachments of the cut ends and another at the antimesenteric ends. Low down in the

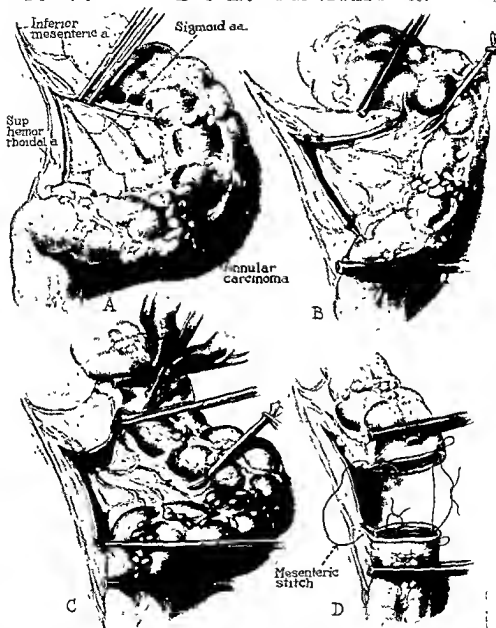


Fig. 1. A-D—The isolation of the lesion and division of the mesentery are shown; the location of the clamps should be noted

pelvis it may be easier to apply the first sutures at either end of the transverse diameter of the bowel. The suture at the mesenteric side is the so called "Mannsell suture." These sutures are illustrated in Fig. 1, *D*. The suture goes through all the coats of the bowel and acts as a brad. The knot is tied on the mucosa, the ends are left long, and a forceps is applied to the long ends,

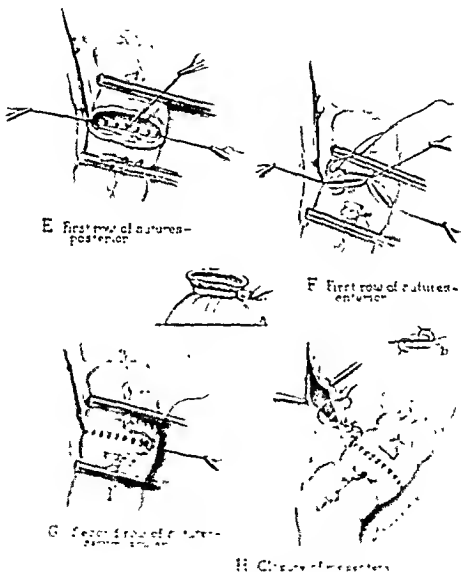


Fig. 1. *E, F*, The principal anastomosis of the posterior and anterior. The first row of sutures at each end of the transverse diameter of the bowel. *G*, The second row of sutures at each end. *H*, Closure of the incisions.



The second suture at the antimesenteric side is a Connell<sup>6</sup> suture through all the coats of the cut ends of the bowel. It is also knotted on the mucosa, the ends left long, and a forceps applied to the long ends.

These sutures are most important. They secure the complete peritoneal covering of the mesenteric attachment of both segments of the gut and also act as guide ropes to help maintain the proper relative position and accurate co-adaptation of the two cut ends.

The two guide sutures are held up by the assistant and the posterior suture line is bisected and then further bisected with carefully spaced through-and-through sutures. The anterior suture line is closed the same way. A second seromuscular row of Lambert sutures is applied.

At all times it is important to have a smooth adaptation of the mucosal surfaces. A mucosal arrangement that creates a flute-valve effect is the most efficacious. Leaks are prone to occur where the mucosal surfaces are not smoothly opposed. This is another argument against the running stitch. Serosa is approximated to serosa, so that no irregular spaces are left. A fine deposition of fibrin seals off the interspaces and produces the most rapid and effective regeneration of tissue. Nicholas Senn,<sup>22</sup> Edward Martin, J. B. Murphy, and others, at the turn of the century, pointed out the great danger of obstruction from too much inversion of the free ends of the gut wall. Murphy demonstrated that a broad serous approximation is not necessary, and that the smaller the bite, the smaller the diaphragm will be.

The more one sutures, the more one strangulates and devascularizes the gut. This leads to leakage at the suture line. There is no need for many sutures, but there is great need for well-disposed sutures (two layers). Excessive zeal in suturing the colon endangers a blood supply which at best is somewhat limited. Small areas of necrosis may develop at the suture line. This devitalization of tissue by strangulation in the field of the ever-present anaerobic bacteria of the colon may encourage a spreading gangrene. Therefore, the use of multiple (three or more) rows of continuous sutures (in the hope that if two are good, more are better) is not only a misconception of the function of suturing and no safeguard at all, but is frequently the instigator of fatal late leaks. The continuous suture stops the blood supply to the cut margins of the colon, and it is on these devitalized margins that the anaerobes flourish.

Safety in colon surgery depends as much upon the integrity of the blood supply as it does on the immediate security against leaks. However, both may be obtained by making an airtight or watertight closure which needs no more than two rows of interrupted sutures for success. The maintenance of sufficient blood supply is the warp and accurate mucosal apposition the woof of a successful anastomosis. Tension at the suture line should be avoided by adequate mobilization of the colon. There should be no pull on the suture line in the long axis of the colon, and what drag there is should be distributed equally around the circumference of the bowel. Tension on the suture line produced by postoperative gaseous distention is prevented by continuous Levine tube suction and the judicious use of the rectal tube. Further, the

application of fine interrupted sutures produces a minimum of tissue devitalization and permits the blood to reach the *fresh, cut noncrushed* margins of the bowel between the interrupted sutures, thus minimizing the danger of necrosis.

Safety in colon anastomosis also depends on the avoidance of crushing or devitalizing tissue in the suture line, and this avoidance is an outstanding feature of the open method of anastomosis which employs fine interrupted sutures throughout.

#### DISCUSSION

There is no attempt here to consider operability rates. A selected series of cases of resectable carcinoma of the colon is presented. The series, however, demonstrates that in cases with no obstruction, resection with primary anastomosis is the procedure of choice (our preference for the open method of anastomosis using two rows of interrupted sutures has been indicated). Further, most patients with partial or even complete obstruction under proper preoperative preparation may become fortunate candidates for resection and primary anastomosis.

In one case carcinoma of the transverse colon was discovered during an exploration of gastric carcinoma. Both the gastric resection and the segmental resection with primary open anastomosis of the transverse colon were performed simultaneously. Once an asymptomatic carcinoma of the sigmoid was discovered during an operation for total hysterectomy. This was nonobstructive and was resected segmentally immediately with primary open anastomosis.

Of the thirty-four cases, four were carcinoma of the right colon, three of the transverse colon, two of the rectosigmoid, one of the splenic flexure, and twenty-two of the sigmoid.

The changing history of resections for carcinoma of the colon has been discussed with emphasis on the modern trend of primary resection. This method flourishes only through the use of the newer concepts of physiology and biochemistry as applied to the pre- and postoperative management of the surgical patient. Some arguments for the open and against the closed methods of anastomosis are presented.

#### CONCLUSION

The shortened hospital stay, the elimination of multiple operations, the savings in time, expense, and psychologic trauma, together with the low mortality (two deaths) in thirty-four cases make the procedure of resection with primary open anastomosis one of choice, or at least one to be recommended highly in resectable, nonobstructive carcinoma of the colon.

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## THE TREATMENT OF ACUTE APPENDICITIS IN A CLOSED CITY

CAPTAIN ALBERT T. HAYS, MEDICAL CORPS, ARMY OF THE UNITED STATES

WHEN Reginald Fitz, Shattuck Professor of Pathological Anatomy in the Harvard Medical School, in 1886 first read his paper on "Perforating Inflammations of the Vermiform Appendix" at a meeting of the Association of American Physicians, he gave to the medical world its first clear-cut description of the pathologic process, the symptoms, the clinical findings, and suggested treatment of a disease which, although previously described, had not been clearly understood until that time, and as a result, not properly treated.

Although thousands of papers have been presented on this subject since then, little has been added to his original description and advice. Mortality statistics in this disease have been reduced since that time with the advances of surgery and its technique. In recent years chemotherapy with the sulfonamide drugs and penicillin have lowered still further our mortality in appendicitis, especially those cases with perforation and peritonitis. It is not my purpose in this paper to present anything new in the way of diagnosis, technique, or chemotherapy, but to discuss the treatment of appendicitis, and the success which was attained in a closed city where such a disease could be treated in its most ideal manner. The early recognition and diagnosis of appendicitis as described by Fitz, and immediate operation once the diagnosis is made as suggested by him and a contemporary surgeon of his time, Alfred Worcester, still stand paramount today as much as in 1886 in the successful treatment of appendicitis.

To quote a few sentences from Fitz's paper and some remarks of his colleague, Worcester:

Fitz recorded "A simple catarrhal appendicitis is to be recognized anatomically, but it is doubtful whether its clinical appreciation is possible. This appendicitis, in the absence of a concretion or foreign body, may progress toward ulceration, even to peritonitis, which may terminate fatally. In the presence of a foreign body or concretion, these events are of likely occurrence. On the one hand, the inflammation may result in the more or less complete obliteration of the canal of the appendix with or without circumscribed dilation. On the other, the ulcerative process becomes associated with a necrosis of the wall, a peritonitis, usually circumscribed at the onset, and perforation."

In respect to diagnosis after discussing the obscurity and variance in appendicitis he stated, "The presence, therefore, of the symptoms now to be mentioned in whom the history of one and particularly several such attacks is to be obtained, is of marked importance in aiding in diagnosis." He found, "that the majority of cases of resulting peritonitis began in the second, third, and fourth days after the inflammation of the appendix is established."

Worcester, who became an advocate of immediate operation as soon as a diagnosis could be made, maintained that "it is impossible to tell what cases are going to be bad." Also, he thought "that the physician should from the begin-

ning, place the responsibility upon the surgeon—because, the end of the first day is later than the end of the first week in some cases."

At the closed, wartime, secret atomic city of Oak Ridge, Tenn., the situation has been unique and unusual. The results in acute surgical conditions of the abdomen, especially acute appendicitis, have been exceptionally good. It is felt that good results have been achieved because of an unusual setup by which it has been possible to treat such a disease in its ideal manner. From December, 1943, to December, 1945, the surgical department has done 357 appendectomies for appendicitis with no mortalities. Oak Ridge has been a closed city of 25,000 to 75,000 population with a limited and centralized medical personnel. The personnel for the greater part has been a group of men trained in their various specialties. Consultation by men trained in surgery, medicine, pediatrics, and gynecology has been available for each and every case and at any time. A call rotation has permitted surgery at any time of the day or night without undue strain on any one surgeon. In short, it has been possible to carry out, idealistically, the treatment of appendicitis in a city of all people—not the rich—not the poor—not the whites—not the colored—but all in the same manner.

**Staff.**—The 357 appendectomies were performed or assisted in by 10 surgeons; 352 of these were participated in by a limited group of 6 surgeons (Table I).

TABLE I

SURGEON	APPENDECTOMIES
A	44
B	72
C	69
D	45
E	65
F	57
G	2
H	1
I	1
J	1
Total	357

352 or 98.6%

## DEFINITIONS

Of the 357 cases, pathologic findings were reported in all but 13. As will be seen later, because of the close correlation between operative findings and the pathologic findings, these were included in the subsequent statistics according to their operative reports, namely, 8 cases of acute appendicitis and 5 cases of normal appendices.

**Acute Suppurative or Gangrenous Appendicitis.**—One group includes those appendices found on pathologic examination to have suppurative inflammation with infiltration of polymorphonuclear cells invading the walls or an actual necrosis of the walls of the appendices.

**Perforated Appendix With Peritonitis.**—One group includes those gangrenous appendices which have actually sustained a perforation of the walls, with pus in the peritoneal cavity either free (generalized), or walled off (localized or abscess). It does not represent those cases which show a localized peritonitis as a result of contiguity to an inflamed organ, nor that group in which there is a clear but cell-containing fluid in the peritoneal cavity.

*Subacute, Recurrent, Chronic, Sclerotic.*—One group includes those appendices which by means of cellular elements or fibrotic changes seen in the walls show signs of subacute or receding inflammation or changes resulting from previous inflammatory processes.

*Normal Appendices.*—One group includes those appendices which show no signs of inflammatory process recent or past and are essentially normal in all respects.

## SEX

Of the 357 appendectomies, 200 were performed on males and 157 on females.

*Males.*—Of the 200 males, 123, or 61.5 per cent of them, had pathologically acute suppurative or gangrenous appendicitis. Seventeen, or 8.5 per cent of them, had perforated appendicitis with peritonitis; of which 7, or 3.5 per cent, had general peritonitis and 10, or 5.0 per cent, had local peritonitis or abscess. Thirty-four, or 17.0 per cent, had subacute appendicitis or sclerotic appendix and 26, or 13 per cent, had normal appendices.

*Females.*—Of the 157 females, 54, or 34.4 per cent, had acute, suppurative or gangrenous appendicitis; 6, or 3.8 per cent, had perforated appendicitis with peritonitis, of which 5, or 3.1 per cent, had general peritonitis and 1, or 0.7 per cent, had local peritonitis or abscess; 44, or 28.0 per cent, had subacute appendicitis or sclerotic appendix and 53, or 33.8 per cent, had normal appendices.

TABLE II. SEX DISTRIBUTION

		Males		357 Cases 200 cases		56%						
		Females		157 cases		44%						
		Perforated with peritonitis						Subacute sclerotic		Total		
		Acute, suppurative		General		Local				Normal		
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	
Males	123	61.5	7	3.5	10	5.0	34	17.0	26	11.0	200	100
Females	54	34.4	5	3.1	1	0.7	44	29.0	53	33.8	157	100
Pathologically Involved Appendices												
278 cases—78%												
Acute, suppurative or perforated						Subacute, sclerotic				Total		
Male	140	(70.0%)				31	(43.5%)		174	62.6%		
Female	60	(30.0%)				44	(56.5%)		104	37.4%		
		200				78						
Normal Appendices												
79 cases—22%												
		Males		26 cases		32.9%						
		Females		53 cases		67.1%						

Of the acute suppurative, gangrenous, and perforated appendices, 70.0 per cent were in males and 30.0 per cent in females. Of the subacute sclerotic group, 43.5 per cent were in males and 56.5 per cent in females. Of the normal appendices, 32.9 per cent were in males and 67.1 per cent in females (Table II).

## PREVIOUS ATTACKS

In review of the histories of these cases definite information concerning previous attacks could be recorded in only 195 cases. In acute, suppurative,

ganglionous, or perforated appendicitis 68.6 per cent of the patients had had previous attacks. In subacute recurrent or sclerotic appendicitis 76.9 per cent had had previous attacks. In appendices found to be normal 70.2 per cent gave histories of having similar symptoms previously (Table III).

TABLE III. HISTORY OF PREVIOUS ATTACKS

	NONE			ONE OR MORE				NO EFFORT			TOTAL
	M	F	T	M	F	T	PERCENT	M	F	T	
Acute, suppurative perforated	25	5	30	45	21	66	64.6	71	33	104	290
Subacute, recurrent sclerotic	7	5	12	18	22	40	76.9	9	17	26	78
Normal	8	6	14	4	29	33	70.2	13	19	32	79
Total	40	16	56	67	72	139		93	69	162	357

It will be noted that in acute appendicitis there is a high percentage of previous attacks and this is especially so in those cases which show signs of changes from previous inflammation.

It is also interesting to note that 70.2 per cent of those patients found to have normal appendices also gave histories of previous attacks of similar symptoms, which adds to the difficulties in differentiating these from true appendicitis in the clinical diagnosis. However, it is evident that appendicitis is a disease which recurs and that a history of previous attacks or symptoms is significant.

From here on the discussion will not include the group of 79 cases which were found to be normal on pathologic examination and only the 278 cases found to have pathologic involvement will be dealt with. However, I wish to comment that, in the successful treatment of appendicitis, a certain number of abdomens will have to be opened in exploration when acute appendicitis cannot be ruled out definitely by clinical means. Some of these were surgical abdomens although the appendix was found to be normal. Five cases of Meckel's diverticulum, one with perforation, are in this group. An abscess of the wall of the cecum is another case and a perforated peptic ulcer is still another. This is especially true in women where the differentiation between pelvic pathology and acute appendicitis is almost impossible at times.

## SEASONAL DISTRIBUTION

Findings show that appendicitis has no seasonal variations. It occurs with about equal frequency during all seasons of the year and bears no particular relation to the seasons for upper respiratory disturbances or enteritis (Table IV).

TABLE IV. SEASONAL DISTRIBUTION OF APPENDICITIS

SEASON	ACUTE SUPPURATIVE PERFORATED		SUBACUTE SCLEROTIC		TOTAL	
	NUMBER	PERCENT	NUMBER	PERCENT	NUMBER	PERCENT
Spring (March, April, May)	47	23.5	24	20.5	70	25.2
Summer (June, July, Aug.)	51	25.5	21	30.8	75	27.0
Fall (Sept., Oct., Nov.)	49	24.5	21	26.9	70	25.2
Winter (Dec., Jan., Feb.)	53	26.5	10	12.8	63	23.0

TABLE V DURATION OF SYMPTOMS

DURATION	MALES	FEMALES	TOTAL	PER CENT
<i>Acute, Suppurative or Gangrenous Appendicitis</i>				
2 hr or under	1	1	2	1.1
2-8 hr	27	8	35	19.8
8-16 hr	36	20	56	31.6
16-24 hr.	16	8	24	13.6—66.1
24-36 hr	17	4	22	12.4—78.5
36-48 hr.	5	2	7	4.0
48-72 hr	9	6	15	8.5
72-96 hr	6	3	9	5.1
4 days and over	6	1	7	4.01
Total	123	54	177	

## GENERAL PERITONITIS LOCAL PERITONITIS

DURATION	MALES	FEMALES	MALES	FEMALES	TOTAL	PER CENT
<i>Perforated Appendicitis With Peritonitis</i>						
2-8 hr	1	0	1	0	2	8.7
8-16 hr	0	0	1	0	1	4.3
16-24 hr.	0	2	1	0	3	14.0—26.1
24-36 hr	3	1	2	0	6	26.1—52.2
36-48 hr	0	1	0	0	1	4.3
48-72 hr	1	1	1	1	4	17.4
72-96 hr	1	0	1	0	2	8.7
4 days and over	1	0	3	0	4	17.4
Total	7	5	10	1	23	

DURATION	MALES	FEMALES	TOTAL	PER CENT
<i>Subacute Recurrent or Sclerotic Appendicitis</i>				
2 hr or under	2	0	2	5.0
2-8 hr	5	0	11	14.1
8-16 hr	4	4	8	10.3
16-24 hr	4	2	6	7.7—24.6
24-36 hr	7	11	18	23.1—57.6
36-48 hr	1	1	2	2.6
48-72 hr	2	7	9	10.5
72-96 hr	3	4	7	9.0
4 days and over	4	4	8	10.3
Interval	3	4	7	9.0

## DURATION OF SYMPTOMS

As mentioned previously one of the most important factors in the successful treatment of acute appendicitis is the possibility of being able to see a patient early in the course of the disease. This allows early recognition or diagnosis and prompt surgical removal.

Of all the patients in this series, 66.1 per cent with acute or suppurative appendicitis were seen within the first twenty-four hours, and within the first thirty-six hours this figure jumped up to 78.5 per cent. Of the patients with perforated appendicitis with peritonitis, 26.1 per cent were seen within twenty-four hours of the onset and 52.2 per cent were seen within thirty-six hours. It can be seen that even a delay of twelve hours in a progressing suppurative or gangrenous appendicitis can increase markedly the percentage of perforation. Of the subacute or sclerotic group the distribution of the duration of symptoms was more variable as might be suspected (Table V).

## AGE DISTRIBUTION

The age distribution showed nothing unusual to the general run for acute appendicitis. 72.5 per cent of the cases of acute suppurative or perforated



appendicitis occurred in the age group of 30 years and under, with 54.5 per cent of all the acute suppurative or perforated cases occurring in the 16 to 30 year group. Also, the subacute recurrent or sclerotic cases are most common in these age groups with 74.4 per cent of them occurring at the age of 30 years or under. They are, however, less common in the first three age groups up to 16 years of age. The youngest patient was 3 years old and the oldest 66 (Table VI).

TABLE VI. AGE DISTRIBUTION OF APPENDICITIS

AGE GROUP	ACUTE SUPPURATIVE		PERFORATED WITH PERITONITIS				TOTAL	PERCENT
	MALE	FEMALE	GENERAL		LOCAL			
			MALE	FEMALE	MALE	FEMALE		
3-5 yr.	2	0	1	0	0	0	3	1.5
6-10 yr.	8	5	2	0	0	0	15	7.5
11-15 yr.	14	3	0	1	0	0	18	9.0
16-20 yr.	13	15	0	1	1	0	30	15.0
21-25 yr.	26	12	0	0	1	1	40	20.0
26-30 yr.	27	8	1	0	3	0	39	19.5-72.5
31-35 yr.	11	5	1	0	3	0	20	10.0
36-40 yr.	0	3	1	0	0	0	13	6.5
41-45 yr.	7	0	0	1	1	0	9	4.5
46-50 yr.	6	2	0	0	1	0	9	4.5
56-60 yr.	0	1	1	1	0	0	3	1.5
61-65 yr.	0	0	0	0	0	0	0	0.0
66 yr. and over	0	0	0	1	0	0	1	0.5
Total	123	54	7	5	10	1	200	

AGE GROUP	MALES	FEMALES	TOTAL	PERCENT
<i>Subacute Sclerotic Appendicitis</i>				
3-5 yr.	0	0	0	0.0
6-10 yr.	1	2	3	3.8
11-15 yr.	1	1	2	2.6
16-20 yr.	5	16	21	26.9
21-25 yr.	6	17	23	29.5
26-30 yr.	6	3	9	10.5-74.4
31-35 yr.	7	1	8	7.7
36-40 yr.	5	2	7	9.0
41-45 yr.	1	2	3	3.8
46-50 yr.	1	0	1	1.3
51-55 yr.	2	0	2	2.6
56-60 yr.	0	0	0	0.0
61-65 yr.	1	0	1	1.3
66 yr. and over	0	0	0	0.0
Total	34	44	78	

## TREATMENT

*Incisions.*—McBurney incisions were used in 255 cases, 167 times in males and 88 times in females. Right rectus incisions were used in 90 cases, 29 times in males and 61 times in females. Various other incisions were used in the remaining 12 cases (Table VII).

*Treatment of the Appendical Stump.*—In those cases reported the appendical stump was inverted with a purse-string suture in 188 cases or 58.4 per cent, and merely tied off without inversion in 134 cases or 41.6 per cent (Table VIII).

*Drainage of the Abdomen.*—The abdomen was drained in twenty-four patients. Seven of these were in nonperforated cases where it was used as a

TABLE VII. OPERATIVE INCISIONS

	MALE	PER CENT	FEMALE	PER CENT	TOTAL	PER CENT
McBurney	167	83.5	88	56.1	255	71.4
Right rectus	29	14.5	61	38.9	90	25.2
Midline	0	0.0	2	1.3	2	3.4
Gridiron	1	0.5	1	0.6	2	
Left rectus	0	0.0	2	1.3	2	
Herniorrhaphy	2	1.0	0	0.0	2	
No report	1	0.5	3	1.9	4	
Total	200	100.0	157	100.0	357	100.0

TABLE VIII. TREATMENT OF THE APPENDICAL STUMP

Inverted with purse string	188
Tied, with no inversion	134
No report	35
Total	357

safety measure. In the perforated cases drainage was used seventeen times, or 73.9 per cent of the cases. It was used seven times in perforated appendicitis with general peritonitis, or in 58.1 per cent of these cases, and ten out of eleven times in the cases of perforation with local peritonitis or abscess, or in 90.0 per cent of these cases. In a total of six cases of perforated appendicitis with peritonitis closure was without drainage, five with general peritonitis and one with local peritonitis (Table IX).

TABLE IX. DRAINAGE OF THE ABDOMEN

	DRAINED	PER CENT	NOT DRAINED	PER CENT
Acute, suppurative gangrenous, not perforated	7	4.1	163	95.9
Perforated appendicitis with local peritonitis	10	90.9	1	9.1
Perforated appendicitis with general peritonitis	7	58.1	5	41.9

*The Use of Chemotherapy in Appendicitis.*—In discussing the use of chemotherapy only the acute suppurative, gangrenous, and perforated cases will be included, namely, those cases in which we might look for something significant in the way of benefit received in the form of lowered mortality or morbidity in actual suppurative conditions. Of the 200 cases of acute suppurative or gangrenous appendicitis and perforated appendices with peritonitis 117 patients, or 58.5 per cent, received chemotherapy in some form, and 83, or 41.5 per cent, received no chemotherapy whatever. Of these 117 patients, 90 received sulfonamide alone, 7 received penicillin alone, and 20 received combinations of sulfonamide and penicillin (Table X).

#### COMPARISON OF CLINICAL DIAGNOSIS, OPERATIVE FINDINGS, AND PATHOLOGIC DIAGNOSIS

Of the 322 cases diagnosed clinically as acute appendicitis or perforated appendicitis with peritonitis, 221 were so diagnosed on operation, of which 192 were so diagnosed pathologically. In other words 192, or 86.8 per cent, of those

TABLE X CHEMOTHERAPY USED

	ACUTE SUPPURATIVE	PERFORATED PERITONITIS	TOTAL
Sulfa Alone			
Locally	58	1	59
Systemically	6	3	9
Locally and systemically	17	5	22
Total	81	9	90
Penicillin Alone			
Locally	0	0	0
Systemically	6	0	6
Locally and systemically	1	0	1
Total	7	0	7
Sulfa and Penicillin Combined			
Locally	0	0	0
Systemically	4	2	6
Locally and systemically	4	10	14
Total	8	12	20
		(58.3%)	
No Chemotherapy	81	2	117
Total		(41.5%)	83
		(20%)	

appendixes diagnosed at the operating table as being acute or suppurative appendicitis were so found on pathologic examination.

Of the ninety-nine cases called normal at the operating table only seventy-four, or 75.7 per cent, were diagnosed as showing no pathology on microscopic examination. It was because of this close correlation between the pathologic diagnosis and the operative diagnosis that the thirteen cases in which no pathologic report could be found were included in the final statistics of these cases, assigning them according to their operative findings as eight cases of acute appendicitis and five normal appendixes (Table XI).

#### HOSPITAL STAY OR MORBIDITY

Before starting the discussion on hospital stay it is to be considered that the greater part of those patients receiving chemotherapy were sicker clinically

TABLE XI COMPARISON OF CLINICAL DIAGNOSIS, OPERATIVE FINDINGS, AND PATHOLOGIC DIAGNOSIS

	CLINICAL DIAGNOSIS	OPERATIVE FINDINGS	PATHOLOGIC DIAGNOSIS
Acute suppurative gangrenous	311	194	192
Perforated with general peritonitis	8	12	---
Perforated with local peritonitis	3	11	---
Subacute recurrent sclerotic	37	28	78
Normal	0	99	74
No report	0	9	17
Total	357	357	357

357 Appendectomies

278 or 78 per cent pathologically involved

79 or 22 per cent normal

278 Pathologically involved appendixes

177 or 63.7 per cent acute suppurative appendicitis

27 or 8.3 per cent perforated appendicitis with peritonitis

78 or 28.0 per cent subacutely involved or showing sclerotic changes

TABLE XII AVERAGE HOSPITAL STAY OF APPENDICTOMY PATIENTS WITH PATHOLOGIC DIAGNOSIS OF NORMAL APPENDIX

	MC BURNEY INCISION (46 CASES)	RIGHT RECTUS INCISION (30 CASES)
Average hospital stay	7.2 days	9.5 days
Shortest stay	3 days	6 days
Longest stay	21 days	16 days

from the onset, especially those who received the drugs systemically. In analyzing the hospital stay of these patients the type of incision used is taken into consideration, the part which chemotherapy may or may not have played in lessening their morbidity, and also those cases of peritonitis in which drainage was or was not used. The discussion will deal with those cases of acute suppurative appendicitis and perforated appendicitis with peritonitis. However, for comparison the average hospital stay of those patients in whom the appendix was found to be normal or subacutely inflamed or sclerotic will be presented first (Tables XII and XIII).

TABLE XIII AVERAGE HOSPITAL STAY OF APPENDICTOMY PATIENTS WITH PATHOLOGIC DIAGNOSIS OF SUBACUTE APPENDICITIS OR SCLEROTIC APPENDIX

	MC BURNEY INCISION (45 CASES)	RIGHT RECTUS INCISION (20 CASES)
Average hospital stay	7.4 days	10.5 days
Shortest stay	2 days	7 days
Longest stay	27 days	14 days

*Patients With Acute Suppurative or Gangrenous Appendicitis*—In acute suppurative or gangrenous appendicitis the average length of hospital stay for all patients receiving chemotherapy of any sort was for those with McBurney incisions 7.7 days and for those with right rectus incisions 9.0 days. In those patients receiving no chemotherapy whatsoever, those with McBurney incisions stayed 6.5 days and those with right rectus incisions 8.0 days. The results found in breaking down these figures are shown in Table XIV.

*Patients With Perforated Appendicitis and Peritonitis in Relation to Drainage of the Abdomen*—Cases of perforated appendicitis and peritonitis will

TABLE XIV AVERAGE HOSPITAL STAY IN CASES OF ACUTE SUPPURATIVE OR GANGRENOUS APPENDICITIS

	NUMBER OF CASES	MC BURNEY INCISION (1078)	RIGHT RECTUS INCISION (1045)
Sulfa Drug Alone	51		
Locally	58		
Systemically	6	6.6	8.8
Locally and systemically	17	9.6	12.0
Penicillin Alone	7		
Systemically	6	8.0	11.0 (1 case)
Locally and systemically	1	1.0	---
Sulfa and Penicillin	8		
Systemically	1	7.8	---
Locally and systemically	4	10.0	11.0 (1 case)
All patients with chemotherapy	94	7.7	9.0
No chemotherapy	51	6.5	8.0

TABLE XV. AVERAGE HOSPITAL STAY IN CASES OF PERFORATED APPENDICITIS WITH PERITONITIS IN RELATION TO DRAINAGE

	DRAINED	NOT DRAINED
General Peritonitis (12 cases)		
McBurney Incisions (9 cases)	6 cases	3 cases
Shortest stay	8 days	6 days
Longest stay	23 days	18 days
Average stay	13.8 days	10.3 days
Right Rectus Incisions (3 cases)	2 cases	1 case
Shortest stay	15 days	
Longest stay	19 days	
Average stay	17 days	9 days
Local Peritonitis (11 cases)		
McBurney Incisions (7 cases)	6 cases	1 case
Shortest stay	7 days	
Longest stay	23 days	
Average stay	12.7 days	11 days
Right Rectus Incisions (4 cases)	4 cases	0 cases
Shortest stay	10 days	-
Longest stay	19 days	-
Average stay	15 days	-

be discussed first in relation to drainage of the abdomen and then chemotherapy. In *general peritonitis* drainage was carried out in eight patients, with an average hospital stay of 13.8 days for those with McBurney incisions and 17.0 days for those with right rectus incisions. Drainage was not carried out in four patients, with an average hospital stay of 10.3 days for those with McBurney incisions and 9.0 days (one case) for those with right rectus incisions. In *local peritonitis* or abscess drainage was carried out in ten patients with an average hospital stay of 12.7 days for those with McBurney incisions and 15.0 days for those with right rectus incisions.

Drainage was not carried out in one patient with a McBurney incision who remained in the hospital for eleven days (Table XV).

*Patients With Perforated Appendicitis With Peritonitis in Relation to Chemotherapy*—Cases of perforated appendicitis with peritonitis in relation to chemotherapy also fall into two groups. Of the twelve cases of *general peri-*

TABLE XVI. AVERAGE HOSPITAL STAY IN CASES OF PERFORATED APPENDICITIS WITH GENERAL PERITONITIS

	NUMBER OF CASES	SHORTEST STAY (DAYS)	LONGEST STAY (DAYS)	AVERAGE STAY (DAYS)
McBurney Incision Cases				
Sulfa drug locally	1	--	--	7.0
Sulfa locally and systemically	2	6	18	12.0
Sulfa and penicillin locally and systemically	5	9	23	15.0
Average length of stay with chemotherapy	8			13.25
Average length of stay with no chemotherapy	1			8.0
Right Rectus Incision Cases				
Sulfa drug systemically	1	--	--	15.0
Sulfa and penicillin locally and systemically	2	9	19	14.0
Average length of stay with chemotherapy	3			14.3
There were no cases in which no chemotherapy was used				

tonitis, chemotherapy was used in eleven cases and no chemotherapy in one (Table XVI). Of the eleven cases of local peritonitis or abscess, chemotherapy was used in ten cases (Table XVII).

It is impossible, of course, to make any significant comparison of the patients with perforated appendicitis with peritonitis who received no chemotherapy with those who did, as this group consisted of only two cases. However, it is felt that the morbidity of those patients with perforated appendicitis with peritonitis who received chemotherapy, namely, 13.25 hospital days and 14.3 hospital days with McBurney and right rectus incisions, respectively, in general

TABLE XVII. AVERAGE HOSPITAL STAY IN CASES OF PERFORATED APPENDICITIS WITH LOCAL PERITONITIS OR ABSCESS

	NUMBER OF CASES	SHORTEST STAY (DAYS)	LONGEST STAY (DAYS)	AVERAGE STAY (DAYS)
McBurney Incision Cases				
Sulfa drug systemically	2	11	23	17.0
Sulfa locally and systemically	1	--	--	17.0
Sulfa and penicillin systemically	2	7	9	8.0
Sulfa and penicillin locally and systemically	2	10	10	10.0
Average length of stay with chemotherapy	7			12.4
There were no cases in which no chemotherapy was used				
Right rectus incision cases				
Sulfa drug systemically	1	--	--	10.0
Sulfa locally and systemically	1	--	--	19.0
Sulfa and penicillin locally and systemically	1	--	--	17.0
Average length of stay with chemotherapy	3			16.7
Average length of stay with no chemotherapy	1			10.0

TABLE XVIII. OVER ALL COMPARISON OF THE AVERAGE HOSPITAL STAY OF ALL PATIENTS WHO HAD APPENDECTOMIES

	MCCURNEY INCISIONS		RIGHT RECTUS INCISIONS	
	CASES	AVERAGE STAY (DAYS)	CASES	AVERAGE STAY (DAYS)
Normal appendices	46	9.2	30	9.5
Subacute sclerotic appendicitis	45	7.4	29	10.5
Acute suppurative appendicitis with no chemotherapy	68	6.5	13	8.0
Acute suppurative appendicitis with chemotherapy	82	7.7	14	9.0
Perforated appendicitis, general peritonitis with drainage	6	13.8	2	17.0
Perforated appendicitis, general peritonitis with no drainage	3	10.3	1	9.0
Perforated appendicitis, general peritonitis with chemotherapy	8	13.25	3	14.3
Perforated appendicitis, general peritonitis with no chemotherapy	1	8.0	0	---
Perforated appendicitis, local peritonitis with drainage	6	12.7	4	15.0
Perforated appendicitis, local peritonitis with no drainage	1	11.0	0	---
Perforated appendicitis, local peritonitis with chemotherapy	7	12.4	3	16.7
Perforated appendicitis, local peritonitis with no chemotherapy	0	---	1	10.0

peritonitis, and 12.4 hospital days and 16.7 hospital days with McBurney and right rectus incisions, respectively, in local peritonitis or abscess, is low for such a serious complication of appendicitis and that the chemotherapy as well as early operation has played a large part in this low morbidity and no fatalities (Table XVIII).

#### CONCLUSIONS

1 The closed city of Oak Ridge has afforded an unusual and an ideal opportunity for the treatment of such a disease as acute appendicitis. The greater majority of the cases, acute, recurrent, and perforated have been seen early in the course of the disease or the particular attack. Consultation has been available, with men trained in their various specialities, at all times in the questionable diagnostic cases. Prompt surgical treatment has been carried out by a constant group of surgeons.

2 It is as true today as it was in 1886, when first brought out by Reginald Fitz, that the most important factor in the treatment of the disease of acute appendicitis is the early recognition and diagnosis of the condition and its prompt surgical treatment. It is as important that the public be educated in the symptoms of this disease as in the infectious and contagious diseases stressed in preventive medicine. It is important that the physician be consulted early and that he recognize the disease which at times can be very vague and deceiving in story and findings. It is important that, in cases in which the diagnosis had not been definitely established, the patient be watched carefully and frequently, as changes in the clinical findings can occur within a short period of time as can the pathologic state of the appendix.

3 In the successful treatment of acute appendicitis a certain number of normal appendices will be removed and exploration of the abdomen done. This is especially true in women in whom pelvic disturbances so simulate appendicitis in their clinical findings that differentiation is impossible. However, the error is greater if one "watches" than if one "looks" when all diagnostic aids have been exhausted and the differentiation cannot be made.

4 Appendicitis is a recurring disease with a history of previous attacks, which in our series was found in 71.6 per cent of the cases, "it is impossible to tell which cases are going to be bad."

5 Chemotherapy, employing sulfonamide drugs alone or in conjunction with penicillin, especially used systemically, has been a definite aid in producing no mortalities and an unusually low morbidity in this series of perforated appendicitis with peritonitis.

6 Chemotherapy does not offer as much in the cases of acute appendicitis without perforation. Local use of the sulfonamide drugs (penicillin not used alone) adds little, if anything, to lessening morbidity or preventing complications. Systemically, both are of value in the more acutely ill patients or toxic cases and in those cases complicated by other infections, as respiratory, kidney, or pelvic.

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## INCOMPLETE REMOVAL OF THE CYSTIC DUCT AS A FACTOR IN PRODUCING POSTCHOLECYSTECTOMY COMPLICATIONS

N. FREDRICK HICKEN, M.D.,\* L. B. WHITE, M.D.,\* AND Q. B. CONAY, M.D.  
SALT LAKE CITY, UTAH

**W**HENEVER the gall bladder becomes diseased, the pathologic process invariably spreads to the cystic duct and may often involve other biliary radicals. Frequently it is the disturbance of cystic duct function which not only aggravates the existing cholecystopathy but may initiate the distressing symptoms which require remedial surgical therapy. For example, a mildly diseased gall bladder may harbor a small calculus without provoking distressing symptoms but if that stone becomes impacted in the cystic duct then acute biliary colic may ensue. Again, a gall bladder may possess normal secretory and absorptive functions but kinks, adhesions, or anatomic deformities of the cystic duct can so obstruct the flow of bile that disconcerting syndromes result.

If this premise be correct then the entire cystic duct should be removed along with the diseased gall bladder. While most surgeons insist that they comply with rule, there are but few who appreciate how frequently it is violated. Beye,<sup>1</sup> in 1936, reported fourteen instances in which long residual cystic ducts had become so dilated as to resemble "reformed gall bladders," and they produced such serious disturbances as to necessitate secondary operations. Best & Hicken<sup>2</sup> emphasized the role of the "residual cystic duct" in maintaining persistent external biliary fistulas. Later, Macdonald,<sup>3</sup> in an exhaustive and scholarly paper, re-emphasized the fact that an infected cystic duct can produce a series of pathologic changes which may so interfere with choledochal functions as to require subsequent explorations.

Failure to appreciate anatomic abnormalities of the cystic duct contributes to its incomplete removal. Variations in its length, configuration, and relationship to the common hepatic bile duct are very common.

Normally the cystic duct is about 3 or 4 cm. in length and lies between the leaves of the gastrohepatic ligament where it unites with the common hepatic bile duct to form the choledochus (Fig. 1). Occasionally, however, the cystic duct may be short so that the gall bladder seems to empty directly into the common hepatic duct. On the other hand, it may be long and tortuous, thus presenting an S-shaped configuration (Fig. 2). At times the cystic duct passes mesially, as if to meet the common hepatic duct, but the two ducts descend together in a contiguous manner until they pass behind the duodenum, where they fuse to form a short, inaccessible common bile duct (Fig. 3). The cystic duct usually empties into the common hepatic duct on its lateral margin, forming an acute angle at their juncture. However, it may empty into the anterior, mesial,

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\*From the Department of Surgery and Radiology of the University of Utah Medical School and the Latter-Day Saints Hospital.





Fig 1.



Fig 2

Fig 1.—The operative cholangiogram gives an accurate picture of the entire biliary system and pancreatic ducts. Note how the cystic duct passes medially toward the common hepatic bile duct, and then descends along its lateral margin before the two unite. If ligated near the gall bladder a long redundant cystic duct is left in situ.

Fig 2.—A postoperative cholangiogram made by injecting a persistent external biliary fistula with diatrizast. Observe the long, dilated, S-shaped cystic duct. This is a striking contrast to that shown in Fig 1. Note the obstructing choledochal stone.

or posterior surface of the common hepatic duct. Macdonald<sup>4</sup> described an instance wherein the cystic duct passed behind the common hepatic duct so as to open into its mesial surface. Reference to Fig. 4 shows how easily ligatures can be placed around the abnormal cystic duct to leave a long redundant stump.

Any abnormalities of the cystic duct can be detected accurately by employing visualizing cholangiograms during the operation. This is accomplished by injecting a solution of 70 per cent diodrast<sup>\*</sup> into the gall bladder lumen and then taking an x-ray view. As the gall bladder and associated biliary radicals will be filled with the contrast medium, an accurate roentgenographic pattern of their size, shape, and relationships will be obtained.



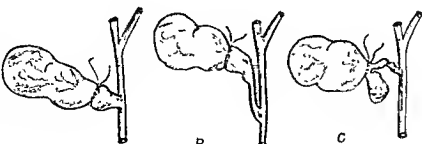
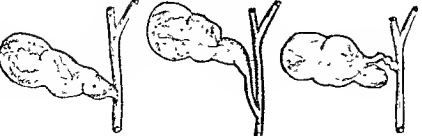
Fig 3—Observe how the cystic duct descends along the lateral margin of the common hepatic bile duct for a distance of 3 cm. before the two fuse

Experience dictates that disturbing dysfunctions of the biliary tract often persist after a cholecystectomy. We have found that the irritative focus is frequently harbored in the remnant of the cystic duct. Corroborative evidence can best be given by submitting representative cases

#### DILATATION OF THE RESIDUAL CYSTIC DUCT—"REFORMED GALL BLADDERS"

Beye<sup>2</sup> appreciated the fact that a long stump of the cystic duct is prone to become dilated as a result of the constant hydrostatic pressure from choledochal bile. The distended cystic ducts resembled small gall bladders and to them he gave the name reformed gall bladders. He admitted that this is not an accurate description of existing pathologic conditions, for the reformed gall bladders do

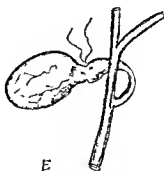
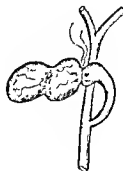
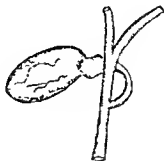
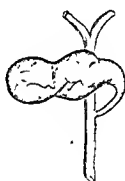
<sup>\*</sup>Diodrast supplied by research Department, Winthrop Chemical Company, Inc., New York, N. Y.



A

B

C



D

E

Fig 4 (For legend see opposite page)

not contain the mucosal or muscular components of the gall bladder. The dilated cystic duct, however, affords an excellent receptacle for bile, but lacking the contractile properties of the gall bladder, it cannot evacuate its contents into the common bile duct. This permits the stagnant bile to disintegrate, thereby favoring the formation of stones.

CASE 1. P. M., a merchant, 66 years of age, had been bothered with "liver troubles" for a period of fifty years, the initial attack following a prolonged case of typhoid fever. A cholecystectomy was performed in May, 1929, following which he was well for eight years. A recurring jaundice aggravated by colicky pains compelled him to submit to a second exploration of the common bile duct on July 16, 1928. The operative records maintain that the

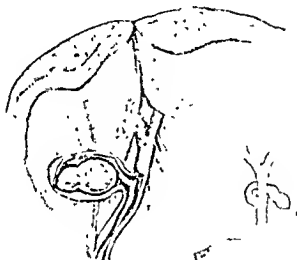


Fig. 5—Inset shows how the cystic duct had herniated through the foramen of Winslow to project into the lesser omental cavity. The main drawing reveals how the cystic duct appeared after being delivered from the lesser omental cavity. Note how it resembles a reformed gall bladder. The impacted cystic duct stone produced a compressive mucocoele which effectively obstructed the common hepatic bile duct.

"choledochus was normal and no cause of the obstructive jaundice was found." However, he continued to have intermittent episodes of jaundice with pronounced pains. On April 6, 1914, the abdomen was opened and an obstruction of the common hepatic bile duct was encountered. In order to determine the nature of this compressive mass a 22 gauge needle was inserted into it and, much to our surprise, we were able to aspirate 12 c.c. of white mucus. In the hope of determining the ramifications of the cystic mass it was injected with 12 c.c. of

Fig. 4—Schematic drawings representing a few of the more common anatomic variations of the cystic duct. If the ligature is placed in the usual position with reference to the common hepatic bile duct, the entire cystic duct, and in many cases a portion of the gall bladder, may be left in situ.

A, Short cystic duct. Ligature includes a portion of the gall bladder and the entire cystic duct. B, Long, descending cystic duct. Ligature includes entire cystic duct. C, Normal cystic duct and dilated pouch of Hartmann. Ligature includes Hartmann's pouch and entire cystic duct. D, A long cystic duct passes anterior to the common hepatic duct before uniting with the mesial margin of the latter. Ligature includes the entire cystic duct. E, Cystic duct passes behind the common hepatic bile duct before uniting with its mesial margin. Ligature includes entire cystic duct.

70 per cent diodrast and a roentgenogram was taken. The resulting cholangiogram revealed the mass to be the dilated cystic duct, a portion of which had herniated through the foramen of Winslow and was protruding into the lesser omental cavity.

After the foramen of Winslow was enlarged by incision of its upper and lower margins, the cystic tumor was extracted from the lesser omental cavity. In Fig 5 is shown how the incarcerated stone had produced a hydrops of the cystic duct, thus causing it to resemble a reformed gall bladder.

The manner in which the redundant cystic duct obtained access to the lesser omental cavity cannot be determined accurately. In all probability it was pushed through the foramen of Winslow during the process of "sponging the gall bladder fossa," at the primary operation. The residual stone so effectively obstructed the cystic duct that a mucocele developed. The abnormal position of the cystic mass permitted it to compress the terminal portion of the common hepatic bile duct. Excision of the cystic duct effected a cure which the two previous operations had been unable to accomplish. This demonstrates the value of cholangiography in determining anatomic abnormalities of the biliary radicals.



Fig. 6.—Cholangiogram made by injecting diodrast into a persistent external biliary fistula. The long S-shaped cystic duct is so dilated that it resembles a reformed gall bladder. Observe the impacted choledochal stone. The small stringlike trickle of diodrast passing through the ampulla of Vater signifies a compressive pancreatitis.

CASE 2.—Mrs F. B., a housewife, 55 years of age, had had a cholecystectomy and several stones removed from the common bile duct. The resulting fistula drained bile for eight weeks. At this time a catheter was inserted into the draining fistula and 23 cc of diodrast were injected into the tube. The resulting cholangiograms outlined an enormously dilated choledochus which was partially occluded by a supra ampullary stone. In Fig. 6 can be noted the thin thread of contrast media, which seeped around the choledochal stone to enter the

ampulla of Vater. This thread pattern is characteristic of an inflammatory pancreatitis. Following these injection studies, the draining fistula healed spontaneously and the patient was discharged by the attending physician.

Six weeks later she was readmitted to the hospital with an intense jaundice. At operation conditions were found as depicted by the previous cholangiograms. The long dilated stump of the cystic duct which resembled a small gall bladder was found to contain "biliary sand." The saccular cystic duct was removed and the choledochus was opened so that the impacted stone could be extracted. Ten days later the postoperative cholangiograms revealed that the pancreatitis had subsided, therefore the drainage tubes were removed. She has been free of all distress during the past two years.

CASE 3.—A farmer, 65 years of age, had had gallstones and gall bladder removed. Following this operation there had been a persistent drainage of bile from the sinus tract for ten weeks. When he was readmitted to the hospital a catheter was inserted into the fistulous tract and 35 cc. of 70 per cent diodrast were introduced. The visualizing cholangiogram not only outlined the dilated cystic duct but also revealed an impacted stone in the ampulla of Vater (Fig. 7). It was interesting to note how the cystic duct descended along the lateral side of the common hepatic duct, the two fusing behind the duodenum to form a short choledochus.



Fig. 7.—The external biliary fistula was injected with 70 per cent diodrast. The cystic duct is so dilated that it resembles a reformed gall bladder. Observe how the cystic duct descends along the lateral margin of the common hepatic bile duct. The common bile duct is obstructed by an overlooked stone.

Apparently the unusual position of the cystic duct caused the first operator to leave the major portion of it behind. The choledochal stone so obstructed the flow of bile that the increased hydrostatic pressure caused the cystic duct to dilate until it resembled a small gall bladder. A cure was effected by excising the fistulous tract and the cystic duct and extracting the impacted stone from the ampulla of Vater. After the common hepatic bile duct was drained for fourteen days, operative cholangiograms demonstrated that the pancreatitis had subsided, therefore all tubes were removed. He has remained well.

#### CYSTIC DUCT STONES

One is annoyed by the frequency with which the stump of the cystic duct harbors elusive calculi which cannot be detected by palpation. The tortuosity

of the duct and the presence of the spiral valves of Heister preclude informative probing, causing the unmolested stones to be left behind to incite undesirable symptoms

CASE 4.—A saleswoman, 58 years of age, had had the gall bladder removed two years prior to the present hospital admission. Since that time she had never been free from gaseous distention, epigastric pain, and jaundice. A second laparotomy revealed an enlarged common bile duct, a dilated and indurated stump of the cystic duct, and diffuse induration of the pancreas. An operative cholangiogram was obtained by injecting 20 cc of 70 per cent diodrast directly into the dilated choledochus (Fig 8). There was dilatation of the entire biliary tree, enlargement of the cystic duct, and obstruction of the ampulla of Vater by a swollen edematous pancreas. So effective was the choledochal obstruction that there was a reflux of



Fig 8.—The operative cholangiogram reveals a dilated stump of the cystic duct. The head of the pancreas is so swollen that it is producing a partial obstruction of the ampulla of Vater. Some of the diodrast, however, has escaped into the jejunum. A laparotomy disclosed the dilated cystic duct to contain a small stone. The irritation from the cystic duct calculus apparently initiated a spasm of the sphincter of Oddi which caused a reflux of the irritating biliary secretions into the pancreatic ducts.

diodrast along the duct of Wirsung. The cystic duct was excised and found to contain a small calculus. The choledochus was opened and explored but no stones could be found. Apparently the cystic duct stone had produced a spastic contraction of the sphincter of Oddi, causing a reflux of the irritating bile along the pancreatic ducts, thus producing an acute pancreatitis. She made an excellent recovery and has been free of symptoms since the operation.

CASE 5.—A woman, 50 years of age, had complained of recurring attacks of colic and jaundice. Two years prior to the present hospital admission a gall bladder containing many small stones had been removed. She was well for two months then she experienced a return of both pain and jaundice. At the second exploration a dilated stump of the cystic duct was found containing a dumbbell-shaped calculus. One end of the stone protruded into the common hepatic bile duct to produce a complete biliary obstruction (Fig 9). Further exploration demonstrated the presence of three stones in the common hepatic duct. Excision of the cystic duct and removal of the offending calculi alleviated all symptoms.

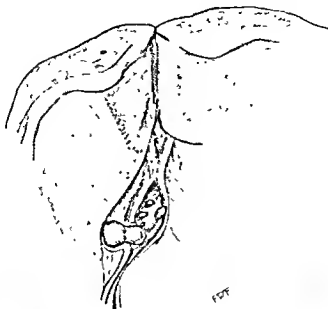


Fig 9—The stump of the cystic duct contains a dumbbell-like stone which protrudes into and obstructs the common hepatic bile duct. Observe the three small stones lodged above the cystic duct calculus.



Fig 10—The external biliary fistula was injected with 70 per cent diodrast, thus visualizing redundant cystic duct and choledochal stone. It is interesting to note the kinking obstruction of the common hepatic bile duct caused by the traction of the cystic duct.



## TRACTION KINKING OF THE COMMON HEPATIC BILE DUCT

A long residual cystic duct presents another hazard by exerting undue traction on the main bile ducts thereby effecting an obstruction. Not infrequently the free end of the cystic duct becomes firmly attached to the ventral surface of the liver, to the duodenum, or to the colon. As cicatricial shortening takes place the traction becomes more intense and so distorts the contour of the common hepatic bile duct that a kinking obstruction may ensue.

CASE 6.—A woman, 13 years of age, had had the gall bladder removed three months previously. She had been annoyed by the persistent drainage of bile from a biliary sinus. During the past month she had complained of recurring paroxysms of biliary colic. In order to visualize the biliary radicals the external fistula was injected with 70 per cent diodrast and an x ray view was taken (Fig. 10). The long cystic duct had produced a traction kinking of the common hepatic bile duct and the ampulla of Vater was obstructed by an impacted stone. At the second operation the dilated common hepatic duct was so distorted by the lateral traction of the cystic duct that it formed an acute angle with the choledochus. The ampullary stone did not effectively block the choledochus as perfusion solutions readily entered the duodenum. The choledochal stone was removed, the cystic duct was excised, and the common hepatic duct was freed from its cicatricial bed, thereby replacing it in proper alignment. She made a most pleasing recovery.

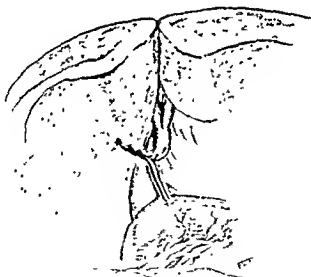


Fig. 11.—Drawing representing a kinking obstruction of the common hepatic bile duct caused by the persistent traction of the stump of the cystic duct as it had become attached to the ventral surface of the right lobe of the liver.

CASE 7.—A man, 56 years of age, had had a cholecystectomy five years previously. He was well for two years then stated that "my gall bladder trouble returned." During the past year he had several attacks of painless jaundice. A second laparotomy disclosed a fibrotic stump of the cystic duct attached to the ventral surface of the right lobe of the liver (Fig. 11). It was exerting so much traction of the lower end of the common hepatic duct that an ob-



Third, we feel it is the obligation of every surgeon to determine the functional integrity of the choledochus and the common hepatic bile ducts before closing the abdomen. Failure to palpate the intraductal stones affords no assurance that they are not present. Even surgical exploration may fail to locate these elusive calculi. Fortunately, errors of omission can be minimized greatly by exploration of the entire biliary system roentgenographically while the patient is still on the operating table. Pathologic abnormalities are detected easily and corrective operations can then be employed. This tends to minimize the need for repetitious operations. The technique of cholangiography is simple and has been described in previous publications. Walters and Thiesen,<sup>8</sup> Macdonald,<sup>6</sup> Best and Hicken,<sup>1</sup> Mirizzi,<sup>7</sup> and Hicken and co-workers<sup>3,4,5</sup> have utilized such studies for a number of years.

#### SUMMARY

Annoying biliary dysfunctions, which persist after cholecystectomy, are often caused by an irritative focus located in the residual stump of the cystic duct. Representative cases of reformed gall bladders, stones in the stump of the cystic duct, persistent external biliary fistulas, and traction kinking of the larger bile ducts are presented to demonstrate how the diseased cystic duct can and does produce these undesirable sequelae.

It is surprising to see how frequently the surgeon fails to remove the diseased cystic duct thus permitting the pathologic process to spread to the larger bile ducts. Certain anatomic abnormalities of the cystic duct, such as variations in its length, configuration, and relationship to the common hepatic bile duct, account for its incomplete removal. Operative cholangiograms accurately visualize existing ductal abnormalities thereby permitting the surgeon to excise the entire cystic duct.

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## CAUSALGIA

A REVIEW OF ITS CHARACTERISTICS, DIAGNOSIS, AND TREATMENT

CAPTAIN JOHN W. KIRKLIN, CAPTAIN ARTHUR I. CHENOWETH, AND  
LIEUTENANT COLONEL FRANCIS MURPHY, MEDICAL  
CORPS, ARMY OF THE UNITED STATES

(From the Neurosurgical Service, O'Reilly General Hospital, Springfield, Mo.)

### DEFINITION AND INTRODUCTION

IT IS the purpose of this paper to review an experience with fifty-two patients suffering from causalgia. In such a study of causalgia, it is imperative that one establish criteria upon which the diagnosis can be made. As remarked by Pollock and Davis,<sup>1</sup> "there is some confusion as to what constitutes a case of causalgia." The original description of the syndrome, by Mitchell, Morehouse, and Keen,<sup>2</sup> is quite specific, and we feel should be followed more strictly. In accordance with this original description, and with the data gathered from our studies, we have formulated a rather strict definition of this condition, which has been employed in our consideration of these cases.

We consider causalgia to be a clinical syndrome associated with a lesion of a peripheral nerve containing sensory fibers, manifested by pain in the affected extremity; this pain is usually of a burning character and is usually located in an area corresponding in general to the cutaneous distribution of the involved nerve. An integral characteristic of this pain, one whose presence is necessary in order to make the diagnosis, is its accentuation by certain disturbing features in the affected individual's environment. There are other aspects of this pain to be discussed more fully later, but the foregoing seems to be a workable definition.

It is obvious that such a definition is a purely arbitrary one, and it is a definition with which many might disagree. We freely admit that there are other painful states associated with injuries to peripheral nerves which some might include under the term causalgia. Some of these other painful states have been referred to as "minor causalgia" by Homans,<sup>3</sup> and as "reflex dystrophies of the extremity"<sup>4</sup> and as "causalgic states"<sup>5</sup> by de Takats, to mention only a few of the many descriptive terms which have been employed. Albeit true that these and other conditions, such as phantom-limb pain, may have the same pathogenesis as causalgia, it seems confusing to employ the term causalgia in reference to them. We arbitrarily have excluded from our group all such cases which do not meet entirely our criteria for the diagnosis of true causalgia. It would probably be preferable to employ a more general term, such as post-traumatic pain syndrome, for these latter cases. We feel that for purposes of accuracy as well as clarification it is preferable to use the term causalgia only in a sharply defined sense.

The term causalgia was first used by Mitchell, Morehouse, and Keen<sup>2</sup> in 1864 in a monograph presenting their experiences with peripheral nerve lesions.

encountered during the Civil War. According to Pollock and Davis,<sup>1</sup> however, as early as 1813 Alexander Denmark had given an accurate description of a clinical condition which was undoubtedly the same as that which was later called causalgia. Since the introduction of the term in 1864, the syndrome has been the subject of articles appearing sporadically in the literature. The enormous volume of peripheral nerve injuries coincident with World War II has provided the material for numerous reports both in this country and abroad. Among these are articles by Spiegel and Milowsky,<sup>2</sup> and Mayfield and Devine.<sup>3</sup> Due to the infrequency with which peripheral nerve injuries are encountered by any one individual in civilian practice, causalgia has in the past not been familiar to the average practitioner of medicine. This is unfortunate, for it is a condition which, when recognized, responds in a gratifying manner to proper therapy. Moreover, once a physician has encountered this condition, he is not likely to forget the haggard, sleepless, pain-racked patient with the causalgic extremity.

The group of patients comprising this study were observed in a series of approximately 2,850 patients with peripheral nerve injuries, who had a total of 3,276 major nerve lesions,\* admitted to the Neurosurgical section in an Army General Hospital in the Zone of the Interior in World War II. This study was aimed at the elucidation of several aspects of the problem, namely, (1) the pathogenesis of the condition, (2) the morphologic lesions found in the involved nerves, (3) the differentiation between causalgia and other post-traumatic painful states in the extremities, (4) the treatment of causalgia, and finally, (5) the factors influencing the results obtained by sympathectomy. No claim is made that anything of positive value has been added to the fundamental understanding of this complex clinical problem. Yet it is believed that such a mass of data upon a relatively uncommon condition and the conclusions derived therefrom are worth recording.

#### MATERIAL AND SOURCE OF DATA

It would have been ideal had we been able to include in this report all cases of peripheral nerve injuries with pain in the involved extremity. Unfortunately, this was not possible because many of the patients who passed through this neurosurgical center had been discharged and their charts were not available. Thus, there have been undoubtedly on our service many cases of mild or perhaps moderate causalgia which are not included in this report. There are probably many other cases of less specific post-traumatic pain which have also been omitted.

We have data, however, on every patient with causalgia or post traumatic pain of a more indefinite nature, who has been subjected to dorsal or lumbar sympathectomy in this hospital. We also have data on a small number of patients with causalgia who for one reason or another were not subjected to sympathectomy. These data comprise the basis for this paper.

This series totals sixty-one cases. In forty nine of these cases the patients were carefully interviewed by us personally, and a complete analysis of their pain, of their nerve injury, and of their response to treatment was possible. We

\*Nerve lesions in the hand were excluded. Brachial plexus injuries were classified as a single nerve lesion.

feel that the data on this group are complete. Most of the material which we shall present is based on this group of forty-nine completely evaluated cases. In addition, there were twelve charts available to us, although the patients themselves had been discharged and could not be interviewed. We have found that even though the progress notes were complete, these charts did not give us sufficient information to allow a complete analysis. Arbitrarily then we decided to use this group of twelve only in evaluating the gross end results of treatment. All other data are based on the group of forty-nine cases alone (Table I).

TABLE I. OVER ALL DATA

Total number of cases	61		
Personally interviewed		49	
Data from records		12	
Total Group	61		
Causalgia		52	
Upper extremity			32
Lower extremity			20
Atypical		9	
Upper extremity			5
Lower extremity			4
Personally Interviewed	49		
Causalgia		40	
Upper extremity			22
Lower extremity			18
Atypical		9	
Upper extremity			5
Lower extremity			4
Treatment of Causalgia			
Sympathectomy	48		
Dorsal		33	
Lumbar		15	
Resection of nerve lesion	5*		

\*One patient was subjected to both sympathectomy and resection of the nerve lesion

#### PATHOGENESIS

Despite the fact that causalgia has been an established clinical entity for a long period of time, and in spite of the widespread attention that the entity has received from numerous investigators, it has remained an inadequately explained syndrome, because of the failure of anyone to provide concrete evidence as to the true physiopathologic nature of the condition. Numerous attempts have been made to explain the pathogenesis of causalgia, but it is to be emphasized that thus far no conclusive explanation has been presented.

Mitchell, Morehouse, and Keen<sup>2</sup> attributed the syndrome to an ascending neuritis affecting the damaged peripheral nerve. Other observers have assigned as the cause of the pain a "neuritis of the periarterial sympathetics," or an "inflammation of the sympathetic fibers in the nerve trunks." It has been stated by some authors that an abnormal vasomotor activity is a causative factor in causalgia. De Takats and his co-workers have, in the past few years, written extensively upon this aspect of causalgia.<sup>4, 8-10</sup> These authors take the view that the syndrome is a vasomotor reflex disorder based, in all probability, upon the axon reflex. De Takats believes that the excitation of efferent vasodilators through the axon reflex produces a humoral substance (probably histamine) at the end organs, which is responsible for both vasodilatation and pain. However,

it should be noted that among the group of cases upon which de Takats bases his conclusions is a wide variety of anatomic lesions and clinical states. Many of these cases, we believe, do not represent true causalgia.

The sympathetic nervous system does seem in some way involved in this condition, as is suggested by many recent observers, although the evidence that this is true is not complete. If it is true, it yet remains to be demonstrated in what manner the sympathetic nervous system is involved. Two possibilities exist: either it plays some role in the production of the pain or it merely serves as the pathway for conduction of the pain. The information at present available does not allow a definite conclusion in this regard.

It can only be admitted that much yet remains to be disclosed in the pathogenesis of causalgia. The facts will come to light only as our knowledge of fundamental physiology and anatomy, including that of the nervous system, is increased.

#### ANATOMIC NERVE LESION

The anatomic lesions in the involved nerves were investigated in all instances possible. Many of the nerves injured in our patients were not explored because they showed spontaneous recovery of function. However, in a little less than one-half of our cases, the involved nerve was explored surgically. Without going into extensive detail, suffice it to say that a great variety of lesions were found in these nerves, none of which differed in any specific regard from the lesions found in a large group of peripheral nerve explorations on patients without causalgia. On gross inspection the appearance of nerves in the causalgic group varied widely. In some nerves there was no demonstrable evidence of damage; in others the lesion appeared to be composed of neuroma and glioma connected only by scar tissue. There were all gradations of lesions between these two extremes, and there was no correlation between the severity of the causalgic pain and the anatomic lesion found.

Obviously the nerves which were without surgical indication for resection were left in situ. However, those showing severe damage with neuroma and glioma formation were on five occasions resected and end-to-end anastomosis was done because of the anatomic lesion found at operation. The nerve ends resected in this small group of cases were studied microscopically.\* The microscopic appearance of these nerves was compared with that of the nerve ends which had been resected in a large number of patients not showing causalgia. No abnormality was found in the causalgic nerves which distinguished them from the specimens resected in patients not suffering from causalgia.

Further, in each of these five cases, silver stents were made of the distal ends and where possible of the fibrous bridge between the neuroma and glioma. In three of these five cases, at operation one or two funiculi (comprising one-sixth to one-eighth of the nerve trunk) were seen on inspection to traverse through the site of injury. For technical reasons, a partial neurorrhaphy was

\*This study was carried out by Major G. D. Ayer, Jr., Chief of the Laboratory Service, O'Reilly General Hospital.

decided against and a total resection was performed. In these three instances, silver stains showed variable numbers of small axons in the distal ends. Examination of the bridge between the neuroma and glioma showed naked funiculi crossing this area. In the other two cases, the neuroma and glioma appeared grossly to be in continuity only by cicatrix. In one in which the bridge could be examined microscopically a few naked fibers were seen crossing it, and some small axons were seen in the cross section of the distal end. In the other, only the distal end could be examined, and this showed many scattered tiny axons.

Considerable care must be exercised in the interpretation of these data. In the three cases in which a few funiculi seemed, on gross examination, to cross the level of injury, it is reasonable to believe that the anatomic lesions were never complete. The other two cases are not so clear, however. There are three possible explanations of the microscopic findings in them. The first is that a few fibers were spared at the time of injury and remained in continuity. The second is that the lesion in these instances was complete at the time of injury, and that subsequently naked fibers grew out from the proximal stump across the cicatrix to enter the distal glioma. The third is that the axons seen in the distal end represent those growing in retrograde fashion from axis cylinders entering the nerve distal to the level of injury. This situation has been found to exist in another instance.<sup>11</sup> Obviously, if the second explanation is the correct one, the causalgia (whose onset in these two instances was immediate) did exist for a time in the presence of a complete nerve lesion. If the third is true, again the syndrome has existed in the presence of a lesion which is locally complete. It is unfortunate that microscopically it is impossible to distinguish among these three possibilities. Thus, we do not know whether the lesion was or was not complete at one time in these two cases. The data indicate, however, that it is not yet conclusively demonstrated that causalgia exists *only* in incomplete anatomic lesions.

In summary then, the only contribution which our data make is that they lay open to question the contention that causalgia occurs only in anatomically incomplete lesions. Our data do emphasize that the lesions may vary tremendously, and that occasionally only a few scattered axons can be found in cross sections and longitudinal sections of the distal end of a nerve which on gross examination appears to have been completely divided.

#### CLINICAL CHARACTERISTICS OF CAUSALGIA

In the majority of cases the causalgic pain began either immediately upon wounding or within a few hours thereafter. Of course, many of the patients were mentally dulled either by the wound or by the sedation at the time of injury, and did not appreciate the pain until eight to twelve hours following injury. For all practical purposes, however, in these men we may consider the pain to have begun immediately. However, in about 20 per cent of the group of forty carefully considered cases of causalgia, the pain began anywhere from three days to four weeks following wounding. In all cases save one, the pain was as severe at the beginning as it ever became, not increasing in severity once it started. In one individual, however, the pain began about seven days



following wounding, became progressively worse during the ensuing two or three weeks, and then remained at constant intensity after that period.

In each patient of this group, except one, the pain was unremitting once it began. Many of the patients noticed variations in the intensity of the pain from time to time, but all save this one stated that at no time after the onset were they completely free of pain. In one individual who meets definitely the causalgia criteria as outlined earlier in this paper, the pain was not constant. In this patient the pain was never present at night and was never present during rainy weather. Other than these times he always had pain.

The type of pain which these patients suffer has been recorded on many previous occasions. It will add little for us to review the literature in this respect, but rather we shall review the types of pain manifested. The description of the pain has been obtained from the patients by personal questioning, care being taken not to prompt them and not to place descriptive words before them. It is important to realize, of course, that the same pain may be variously described by different individuals, due to varying past experiences and varying commands of language. Taking these factors into account, it can still be stated that the type of pain in causalgia does seem to vary somewhat from individual to individual.

It is obvious from Table II that burning is the word most frequently used by patients to describe the pain of causalgia. Sometimes this word is used alone and on other occasions other words such as throbbing, aching, or twisting are used to qualify it. In three instances, however, the patients noted no burning whatsoever, and in eleven instances burning, although present, was a minor feature of the complaint. Throbbing was used with fair frequency to describe the discomfort, although in no instance in either the upper or lower extremity was the pain described as exclusively throbbing. Aching was a prominent feature of the causalgia in a few cases. Three men with upper extremity causalgia described the pain chiefly as one of "pressure, as if someone were wringing the blood out into the ends of the fingers and as if the finger tips were about to burst." Knife-like, stabbing pains and twisting, crushing pains were bitterly complained of by a few of the patients.

It has been stated that the distribution of the pain in causalgia corresponds in general to the cutaneous distribution of the involved nerve. In both the upper and lower extremities approximately 60 per cent of the patients had pain limited strictly to the distribution of the involved nerve. However, roughly 40 per cent had pain in the hand or in the foot not strictly limited to the cutaneous distribution of any one nerve. It is of interest to note that in the group with strict anatomic distribution of the pain, roughly 70 per cent had accompanying complete sensory lesions of a second major nerve in the involved extremity, while in the group with generalized pain only 15 per cent had such accompanying complete sensory lesions. It is possible, then, that the reason for the pain's being strictly localized in certain cases is that an anesthetic area in the affected hand or foot prevents appreciation of pain in areas other than that supplied by the causalgic nerve. On the other hand, in patients with

TABLE II. THE PAIN OF CAUSALGIA

TYPE OF PAIN	UPPER EXTREMITY (% OF TOTAL GROUP)		LOWER EXTREMITY (% OF TOTAL GROUP)	
Burning	90		87	
With burning				
All or mainly burning	57		67	
Some burning	33		20	
Without burning	10		13	
Throbbing	48		13	
With throbbing				
All or mainly throbbing	14		0	
Some throbbing	31		13	
Without throbbing	52		87	
Aching	24		27	
With aching				
All or mainly aching	0		13	
Some aching	15		14	
Without aching	76		73	
"Pressure"				
With "pressure"	14		0	
All or mainly "pressure"	14			
Some "pressure"	0			
Without "pressure"	0		0	
Knifelike, Stabbing	10		31	
With knifelike stabbing				
All or mainly knifelike stabbing	5		31	
Some knifelike stabbing	5		0	
Without knifelike stabbing	0		0	
Twisting, Crushing	14		20	
With twisting, crushing				
All or mainly twisting, crushing	5		7	
Some twisting, crushing	9		13	
Without twisting, crushing	0		0	

\*Not calculated.

generalized pain the lack of any anesthetic area may allow an overflow of the painful sensation to other parts of the extremity.

Another characteristic of causalgia is that in most cases the lesion in the involved nerve is clinically incomplete. Thus, in 72 per cent of the forty patients personally interviewed the paralysis of the involved nerve as indicated by clinical examination of the patient was definitely incomplete. In the remaining 28 per cent the individuals when first seen with causalgia manifested complete motor and sensory paralysis of the involved nerve. A few of these patients spontaneously recovered function at a later date, but the remainder were explored. In some a minimal lesion was found at operation requiring either a neurolysis or no operative treatment. As noted previously, in five instances it was deemed necessary to carry out a resection and neuroorrhaphy.

As has been pointed out, causalgia is associated with a lesion of a peripheral nerve containing sensory fibers. In our experience lesions of mixed nerves have most commonly been associated with the syndrome although occasionally injury to a purely sensory nerve may produce the syndrome. Injury to the median nerve in our group of cases was the most common lesion responsible for the production of causalgia. Injury to the sciatic nerve which involved the tibial component alone was slightly less common. The frequency with which

TABLE III. NERVES INVOLVED IN TOTAL CAUSALGIA GROUP

Upper extremity	32	
Brachial plexus		3
Median		28
Radial		1
Lower extremity	20	
Sciatic (posterior tibial component)		14
Sciatic (peroneal component)		3
Saphenous		3

TABLE IV. LOCATION OF WOUND

Upper extremity	32	
Anilla		9
Upper arm		16
Elbow and forearm		7
Lower extremity	20	
Buttocks		7
Thigh		13
Lower leg		0

other nerves are involved is indicated in Table III.\* The location of the wounds in this group is indicated in Table IV.

#### AGGRAVATIONS AND RELIEFS OF PAIN

A characteristic feature of the pain of causalgia is its aggravation by certain disturbing things which happen around or to the patient. It is our conclusion after examination of the data which we have gathered that this is probably the single most constant feature of the group which we have set aside as true causalgia. By virtue of the very definition which we have adopted, 100 per cent of the patients who we believe suffer from causalgia manifest this tendency to aggravation. Those without it, we have not considered to have causalgia. The precise factors which aggravate the pain vary from individual to individual.

In Table V is indicated in general the type of factors which aggravated the pain in these patients. This table is not broken down into the upper and lower extremities, for there is no significant variation in this respect between the two groups. The patients with lower extremity causalgia, however, tend

TABLE V. AGGRAVATING FACTORS

FACTOR	PER CENT OF CASES AGGRAVATED
Moving or touching involved part	74
Sudden jar	61
Loud noise	58
Emotional excitement	47
Touching slick objects such as bed sheets or paper	28
Touching patient with a dry finger, but not with a wet finger	19
Looking up in the air or at high objects	17
Touching the patient's body at any point	14
The sound of certain words, such as paper or slick	8

\*Since this article was written a patient has been encountered who had an incomplete lesion of the cervical plexus with severe causalgia in the occipital and postsuticular regions of the scalp. He has been completely relieved by dorsal sympathectomy of the type to be described later.

to be somewhat less affected by these factors than are those with upper extremity causalgia. This aspect of the syndrome is a striking one. Dramatic examples are the few individuals in whom the mere sound of the spoken words slick or paper provoked severe exacerbation of the pain. One patient could not tolerate the sound of papers rattling in the bed next to his because of the intense aggravation of the causalgic pain. Another patient had pain more severe than usual during the voyage back from overseas, because the water looked so smooth to him as he gazed upon it. Still another unfortunate victim of this condition developed a tremendous fear of flies, because he was constantly apprehensive lest they alight upon his body and aggravate the constant burning pain in the hand. One of these men could not even look at a picture of a high building without marked increase of pain. These patients not infrequently go to extremes in order to avoid any noise or disturbing factor. In the more severe cases the patients have on occasions locked themselves in an isolated room, put their heads beneath the covers, and refused to talk with anyone who came near them. Of course, some are much less dramatic and merely shield the affected part to prevent one's touching it.

It is important at this point to differentiate the aggravation of causalgic pain produced by touching the affected part from hyperesthesia. Hyperesthesia, in peripheral nerve injuries, is occasionally very pronounced and thus disabling; it is, of course, produced by touching the affected part. This is not causalgia, however, and the failure to distinguish it clearly from causalgia is apparent in much of the recent literature. Furthermore, hyperesthesia is not a necessary concomitant of causalgia, although occasionally they do coexist. In patients afflicted with hyperesthesia, the pain is not constant, is not usually burning in character, and is not aggravated, or in point of fact, produced, by anything except contact with the hyperesthetic part. This distinction is an important, although occasionally difficult, one to make.

Many of the patients with causalgia discovered that certain things would alleviate the pain. The vast majority of them noted that the pain was somewhat alleviated by very quiet surroundings without any disturbing features. Roughly 50 per cent of the men found that wrapping the affected part in a wet cloth was helpful. Most of the men preferred a wet cool cloth rather than a wet warm one, but some did prefer the latter. In a few severe cases of upper extremity causalgia the patients even filled their shoes with water during the day and slept with wet socks on their feet at night because it tended to relieve the pain in the extremity. This, of course, was noted by Mitchell and his collaborators in their original description<sup>2</sup> of the syndrome. Several found that sleeping on smooth sheets and pillow cases was intolerable and requested rough towels or blankets instead. Our data do not indicate that these alleviating factors, which many of the men found, are a really integral feature of the causalgic syndrome. As stated, 50 per cent of the men with otherwise typical causalgia did not find that wrapping the affected extremity in wet cloths or sleeping on rough rather than smooth bedclothes was beneficial.

About 60 per cent of the men with causalgia noted a difference in the pain during the day as contrasted with the night. Of this group about two-thirds

found the discomfort to be partially relieved by nightfall, while about one-third found the pain to become worse at night. It is also interesting to note that some patients found that the pain was worse in hot weather, others in cold weather, while some noted no relation between pain and the temperatures of their environment. There was no correlation whatsoever between the aggravation of the pain by heat or by cold and the preference of hot or cold wet rags on the extremity for the relief of pain. It is apparent from our data that although such things as the time of day and the temperature of the environment do affect the pain in some cases, this is not a constantly aggravating factor such as noise, excitement, sudden jars, and the like.

#### A CONSIDERATION OF ATYPICAL POST-TRAUMATIC PAIN

Having presented the features characterizing true causalgia, we shall now consider briefly other painful post-traumatic states. Such syndromes have been designated by various terms; a few examples are Sudeck's atrophy, post-traumatic angiospasm, minor causalgia, and reflex sympathetic dystrophy. De Takats and Miller<sup>1</sup> have grouped many of these together under the term "reflex dystrophy of the extremities." These authors describe reflex dystrophy as "... severe, persistent pain of a burning character with paroxysmal aggravations, presented by a patient whose injured limb is properly immobilized, non-infected, and seemingly on its way toward a normal course of recovery. . ." Injury to nerves, blood vessels, periarticular structures, and rarely to bone are said to give rise to such a disorder. Further, it has been stated that the condition may develop after a minor injury to an extremity not involving bone, nerve, or a major vessel. The early stages of such a syndrome are characterized<sup>14</sup> by hyperemia, while in the chronic stage, signs of excessive vasomotor activity dominate the picture, with cold, clammy skin and trophic changes in skin and muscles. It is possible that many of the immobile clawlike bands with hard, fibrotic forearm muscles described as classical cases of Volkmann's contracture may represent terminal stages of reflex dystrophy.

Despite the description of reflex dystrophy quoted from deTakats and Miller, most of the cases they reported do not quite fit this description. If they did, then they should probably be considered to be true causalgia. Further, none of the cases quoted in recent literature<sup>2, 6, 8, 10, 12, 13</sup> on this ill-defined group involved constant pain, usually of a burning character, invariably aggravated by disturbing factors in the patients' environment and associated with injury to a peripheral nerve. For this reason, it seems advantageous not to employ the terms causalgia or causalgic to this group at all, but to limit the use of these words to the clearly defined group of cases originally referred to by Mitchell, Morehouse, and Keen. True, causalgia may be related to these other post-traumatic pain syndromes, but it is a clinical entity with sufficient diagnostic criteria to be separated from these other states. Such a sharp differentiation will clarify and simplify, rather than confuse, this entire subject.

We have had no experience with cases entirely similar to those quoted in the articles just mentioned. Furthermore, we have had no experience with post-traumatic pain syndromes in individuals suffering merely vascular, bone,

or soft tissue damage without peripheral nerve damage. As noted previously, such cases have been reported in detail by others. However, we will present in brief a small group of cases of atypical post-traumatic pain, occurring in individuals who have suffered peripheral nerve lesions. Cases such as these must be distinguished from true causalgia.

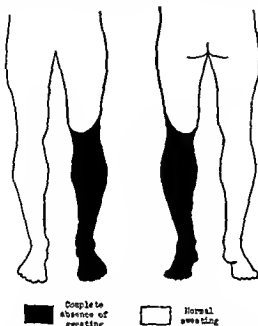


Fig 1—No relief of atypical pain following complete (Grade I) lumbar sympathectomy

In one, the patient had a moderately severe, constant burning pain in the foot following a wound of the popliteal fossa. The pain began immediately after wounding and was constant, but was not aggravated by any of the factors aggravating causalgia. The presence of complete paralysis of the tibial and peroneal nerves caused us to explore these, and the anatomic findings demanded end-to-end anastomosis of both. There was no improvement in the pain. The second and third lumbar sympathetic ganglia were then removed extraperitoneally through a high transverse abdominal incision, postoperative dermatometer readings showed the patient to be completely denervated from the area of the knee distally (Fig. 1). The pain was not improved in the slightest. After six weeks, a resection of the tibial suture line was carried out because of the poor appearance, microscopically, of the nerve ends previously resected, through the same incision a periarterial sympathectomy was performed on the femoral artery at the level of its emergence from the adductor canal. Following these procedures, and continuing to the present time, the patient has been relieved of the constant burning pain. Because of the complete lack of aggravation of the burning pain by noise, excitement, touching the foot, and the like, we do not consider this to be true causalgia.

Three patients were encountered in this group whose chief complaint was that they developed severe pain in the hand of the injured arm while in the cold. These men had varying degrees of minor pain constantly, not aggravated by the factors aggravating causalgia. Dorsal sympathectomy was performed, and following this procedure the men had complete relief of pain when in the cold. Their hands still became abnormally cold in the cool weather, but they were no longer painful.

An atypical post-traumatic pain syndrome was encountered in an individual suffering a simple dislocation of the left shoulder and an incomplete paralysis of the brachial plexus. He had the immediate onset of severe burning, aching pain in the hand. It was not aggravated by any known factor. Because procaine block of the stellate ganglion on three occasions gave complete relief of pain lasting three to thirty minutes, a dorsal sympathectomy was performed. Postoperative dermatometer readings indicated that the sympathectomy was complete. Nonetheless the patient felt that, although he no longer had burning, the over-all discomfort was still so great that he was not significantly improved. Further study revealed a herniated nucleus pulposus in the cervical region, between the fifth and sixth cervical vertebrae on the left side. This was removed surgically, and following this he has shown gradual improvement and is now free of pain. It is our feeling that the pain in this patient was actually the pain of a cervical herniated nucleus pulposus, and was not causalgia, despite its burning, aching character.

In this atypical group of cases, there were three instances of pain in the lower extremity following minor peripheral nerve injury. These individuals had a sharp, stabbing, or aching pain in the foot, inconstant, and aggravated only by walking. Although we did not consider these causalgia, they were subjected to lumbar sympathectomy because they had shown a favorable temporary response to procaine block of the lumbar sympathetic ganglia. Two of these patients showed some improvement following this procedure, and one showed no improvement.

One last case, and a very instructive one, is that of an individual suffering a wound in the upper arm (producing a mild, incomplete paralysis of the median nerve) and wounds of the tip of the thumb and little finger. The only signs of median nerve damage were weakness of the opponens pollicis muscle and hyperesthesia in the distribution of this nerve. However, the patient complained bitterly of pain—not constant pain, but pain “like electric shocks” when anything touched the thumb, index finger, or middle finger. There was no burning and nothing produced this pain except touching these areas. It was so severe that he constantly protected this hand. Because of the mistaken diagnosis of causalgia, a dorsal sympathectomy was performed, which completely failed to relieve the pain. An external neurolysis on the median nerve in the upper arm similarly failed. Finally, the digital nerves in the thumb and middle finger were sectioned, a drastic procedure but one demanded by the patient. This immediately relieved the hyperalgesia, replacing it of course with anesthesia. The nerves to the index finger were not sectioned, and the

patient has learned to tolerate the discomfort in this digit. This case actually was not causalgia, and should not have been confused with it. It represents, actually, a severe hyperesthesia.

In concluding a discussion of these difficult atypical cases, we wish to state that the exclusion of some of these from the causalgia group might be considered an error. However, we have so separated them because the clinical syndromes presented by these men do not meet the requirements we have established for making the diagnosis of causalgia. If further experience proves this wrong, the classification must, of course, be revised.

#### THE TREATMENT OF CAUSALGIA

Causalgia, especially cases of mild or moderate severity, may subside spontaneously within a period of a few months. We have no data, unfortunately, concerning the frequency of this. However, when the condition is moderately severe or severe, procaine block of the sympathetic supply to the involved extremity should be performed. Infrequently, a series of three or four blocks, twenty-four to forty-eight hours apart, will relieve the pain to such an extent that the patient can tolerate it satisfactorily and thus does not require operative intervention. However, in our experience we have found that the pain usually returns to the preinjection level after thirty to sixty minutes, even after two or three successive blocks. It is then useless to persist in this, and one must turn to other methods of treatment.

One method which has been attempted is external or internal neurolysis of the lesion in the involved nerve. It has been stated by some that neurolysis or partial resection of the neuroma may provide relief in some cases, however, this has not been the experience of most workers. In four of our cases, neurolysis of the involved nerve had been done prior to sympathectomy, with no relief of pain in any instance. In general, it seems safe to assert that an external or internal neurolysis cannot be expected to relieve the pain of true causalgia.

However, if, apart from the attendant causalgia, there is an indication for exploration of the peripheral nerve, we believe that the nerve should be explored prior to sympathectomy if the patient feels that he can tolerate the causalgia during the postoperative period, should it not be relieved. On infrequent occasions, as demonstrated in our series, a patient with causalgia may clinically manifest complete paralysis of the involved nerve, associated with a lesion in that nerve which requires resection and neurorrhaphy, in such cases, of course, neurorrhaphy is performed. It has been our experience that such a procedure is sometimes followed by relief of the existing causalgia. This will be discussed in detail later.

Another operative procedure that has received considerable attention in the past is periarterial sympathectomy. This consists of stripping the adventitial sheath of a major vessel to remove the perivascular plexuses of sympathetic nerves in that segment of the vessel. It was popularized by Leriche and other European surgeons in the 1920's, but has never received wide favor in this



country. There is no sound anatomic basis to support the procedure, for the vessels of the extremities have a segmental nerve supply, the sympathetic fibers emerging from the somatic nerves at intervals throughout their course in an extremity. Further, experimental and clinical investigation has revealed that there is no more than a transient increase in blood flow in a limb after periarterial stripping.<sup>14</sup> Yet the procedure has been reported as yielding successful results in some cases. We have had no experience with this procedure in true causalgia.

Unquestionably the method of treatment giving the best permanent results is central sympathectomy. As far as we are able to discover, this was first employed in the treatment of causalgia by Spurling<sup>15</sup> in 1930. Of course, both dorsal and lumbar sympathectomy had been used prior to that in the treatment of certain vasomotor disorders of the extremities. This method of treatment was the basis of our management of the cases comprising this series. The technique of the procedure employed need not be described in detail, although a brief statement on the subject is in order.

The technique that we have used for dorsal sympathectomy is a slight modification of that described by Smithwick.<sup>16</sup> It consists of sectioning the sympathetic trunk below the third ganglion and dividing the gray and white rami between the second and third ganglia and their respective intercostal nerves. The central stump of the sympathetic chain is then sutured into the intercostal muscles below the second rib. The chain is approached through an oblique or paravertebral incision centered over the third rib, with subperiosteal resection of the inner segment of that rib and the corresponding transverse process. The operation leaves the ganglia in place and maintains intact most of the postganglionic fibers to the arm. Furthermore, since the lowest cervical and first dorsal ganglia are not disturbed, a Horner's syndrome is not produced. The procedure resulted in most cases in denervation of the entire arm, and variable portions of the chest, face, and scalp (as indicated by dermatometer readings).

In the case of the lower extremity, it has been our practice to resect the second and third lumbar ganglia, with the intervening sympathetic chain. This has resulted in complete denervation of the lower extremity on the side operated upon, below the level of the thigh. Since the fourth lumbar ganglion, and those ganglia distal to it, are left *in situ*, the postganglionic mechanism again is left intact. We have used the anterior muscle-splitting approach of Pearl<sup>17</sup> and the lumbar approach. It is our impression that the former provides easier access to, and better exposure of, the sympathetic chain than the latter, except in large individuals with thick trunks and heavy abdominal musculature. In three recent instances, a high transverse abdominal incision has been very satisfactorily employed in the extraperitoneal approach to the lumbar ganglia. It is carried from a point roughly 2 cm above and lateral to the umbilicus directly laterally to the level of the anterior axillary line, usually crossing the lower portion of the eleventh rib. The external oblique muscle is cut transversely in the direction of the skin incision, and the remaining layers are split in the

direction of their fibers. Care is taken to aim the split in the internal oblique muscle at a point about three inches cephalad to the umbilicus. This incision seemed to provide a more direct access to the lumbar ganglia to be resected, particularly the second, and thus was perhaps an improvement over the oblique, completely muscle-splitting incision.

In the early part of our experience, it is probable that on some occasions the second lumbar ganglion, and even in a very few instances the third, were not resected, but rather the chain and a ganglion distal to these were removed. This seems an easy pitfall when the anterior oblique incision is used unless care is taken to avoid it. As will be shown later, dermatometer readings bear out this probability. Later, great care was taken to resect with all possible certainty the second and third lumbar ganglia and their intervening chain.

Sympathectomy in either the dorsal or lumbar region is not a difficult procedure. There were no deaths in our series, and few have been reported in the literature. The only complication that has been encountered is pneumothorax, occasionally associated with dorsal sympathectomy, and this, when it occurred, has caused no serious postoperative morbidity. Except in patients who have had previous chest wounds, with thickening and adherence of the pleura, this complication should not occur if the proper care is exercised. Of course, either dorsal or lumbar sympathectomy is a major operative procedure and should not be undertaken without due consideration.

The cases were selected for sympathectomy on the basis of the clinical syndrome. In all instances procaine blocks of the sympathetic ganglia to the involved extremity were carried out preoperatively. In most cases the results from such blocks paralleled the results obtained by sympathectomy. However, in a few instances adequate sympathetic blocks failed to give relief of pain when sympathectomy itself did provide a satisfactory result, and in several individuals sympathectomy did not produce as complete relief as had been temporarily produced by procaine block. Thus, in our hands preoperative blocking of the sympathetic ganglia was of some aid in prognosticating the relief from sympathectomy but was not completely correlated with the results from this procedure. Therefore, it is our conclusion that procaine block is not necessary in making the diagnosis of causalgia, and is not needed in making the decision for or against sympathectomy. However, because of the few instances in which some permanent relief followed several procaine blocks, this procedure probably should be used preoperatively.

An analysis of the results of sympathectomy is presented in Table VI. This over-all analysis includes not only the personally interviewed patients, but

TABLE VI. RESULTS OF SYMPATHECTOMY FOR CAUSALGIA

RESULTS OF SYMPATHECTOMY	PER CENT OF TOTAL GROUP			
	UPPER EXTREMITY		LOWER EXTREMITY	
	PER CENT	NUMBER OF CASES	PER CENT	NUMBER OF CASES
Class I	40	13	33	5
Class II	33	11	27	4
Class III	27	9	33	5
Class IV	0	0	7	1
Total	100	33	100	15

rather the entire series. Class I is comprised of those patients completely relieved of pain by sympathectomy. Class II includes those patients who have an excellent result from sympathectomy with nearly complete relief of pain, but who present a little residual difficulty. Anyone with residual pain of any type, no matter how slight, is included in this group rather than in Class I. Class III includes those patients with definite improvement in the causalgia, but with moderate residual pain. All patients included in this group felt that the sympathectomy was clearly worth while. Class IV is the group of failures from sympathectomy. In this group the patient had either no relief or so little relief that the operation was not worth while.

To summarize, the results of sympathectomy in this condition have been very gratifying. Of forty-eight patients so treated, only one felt the operation was not definitely worth while. On the other hand, less than one-half of the patients had total, complete, relief of pain. It is interesting to note that in all instances following surgery, the factors which once aggravated the pain no longer did so.

We recognize and wish to emphasize that the low percentage of failures from sympathectomy might be directly attributed to the fact that we excluded from the group of true causalgias certain cases which do not meet the criteria which we set down in the beginning of this paper. These cases were discussed previously. It is apparent that these patients responded less well to sympathectomy than those who meet the criteria of true causalgia.

The data were analyzed in an attempt to discover any factors which might indicate preoperatively which patients with true causalgia will have the most complete relief of pain following sympathectomy. Several factors must be considered.

One might inquire first if the type of pain, that is whether it was mainly burning, or aching, or throbbing, influences the result from sympathectomy. A careful attempt to correlate the type of pain with the result of sympathectomy showed absolutely no relation between the two. Some men whose main pain was a "bursting pressurelike" feeling in the finger tips had complete relief from sympathectomy, while others with identical pain had less relief. The same is true of burning or throbbing. Thus, from the type of pain which a man has, one cannot accurately predict the result that will be obtained from sympathectomy. We then tried to correlate the result from sympathectomy with the interval elapsed from the time of wounding to the time of sympathectomy. This again was a total failure and we found no correlation between this interval and the result of operation.

We then analyzed carefully the data concerning aggravation of pain. In order to analyze these data, we graded the aggravation on the basis of I to IV, Grade I being slight aggravation and Grade IV being marked aggravation by anything in the patient's surroundings. Examination of the data in Table VII gives a slight suggestion that those with the more severe aggravations tend to be more completely relieved by sympathectomy than the others. However, the data do not permit any definite conclusion in this regard.

TABLE VII. RELATION OF RESULT OF SYMPATHECTOMY WITH DEGREE OF AGGRAVATIONS

RESULT FROM SYMPATHECTOMY	GRADE OF AGGRAVATION (PER CENT OF TOTAL IN EACH CLASS)				TOTAL
	GRADE I	GRADE II	GRADE III	GRADE IV	
Class I					
Upper extremity	0	25	50	25	100
Lower extremity	20	60	0	20	100
Class II					
Upper extremity	23	11	33	33	100
Lower extremity	25	75	0	0	100
Class III					
Upper extremity	0	67	33	0	100
Lower extremity	17	50	33	0	100
Class IV					
Upper extremity	0	0	0	0	0
Lower extremity	100	0	0	0	100

An extremely important consideration is—have the sympathectomies been adequate in each case? In order to answer this question we have estimated the completeness of the sympathectomy by measurement of the sweating in the involved extremity following surgery. The dermometer,<sup>12</sup> an instrument measuring skin resistance, was employed for this.\* In nearly all these cases we have preoperative as well as postoperative dermometer readings, so that we know the amount of desweating present prior to sympathectomy resulting from the nerve lesion itself. Of course, varying amounts of the head, neck, and chest, as well as the arm, are sympathectomized by the upper extremity procedure, but only the arm data are pertinent and thus are included. Occasionally, following lumbar sympathectomy a portion of the thigh is denervated. However, all observers agree that the removal of the second and third lumbar ganglia usually denervates only the knee area and the lower leg, not the thigh. The estimates of completeness of sympathectomy given here refer, in the case of the upper extremity, to the area of the shoulder and that distal to it; in the leg, they refer to the area of the knee and that distal to it. We have arbitrarily graded the amount of desweating, and thus the completeness of the sympathectomy, in the following manner:

Grade I, Complete desweating of the area

Grade II, No areas of normal sweating, but a few very small scattered areas of slight sweating.

Grade III, Incomplete desweating with some areas of normal sweating.

Grade IV, No change in sweating from preoperative status.

Although one strives always for complete and total desweating, it has been our impression that these patients having Grade II desweating are satisfactorily sympathectomized. Grade III desweating, however, represents a definitely incomplete sympathectomy. In the upper extremity, only one patient tested was classed in Grade III, and this was one in whom the operator had difficulty in identifying the second thoracic sympathetic ganglion, and probably only the

\*These measurements were very kindly made for us by First Lieutenant Ann Martin in the Physical Therapy Department, O'Reilly General Hospital. The Neurodermometer made by A. R. Spartana Co., Baltimore, was employed.

third was decentralized. However, the patient was completely cured of a severe causalgia. In the lumbar group, there were four instances of incomplete sympathectomy; as stated previously, probably the second lumbar ganglion, and perhaps the third, were not removed in these cases. The incompleteness in each instance showed itself as a varying area of normal sweating somewhere in the distribution of the saphenous nerve. One of these patients, operated upon recently and on whom this error should not have been made, showed no relief of pain following sympathectomy. Subsequent exploration of the tibial nerve in this patient disclosed a lesion which necessitated resection and neurorrhaphy; no relief in the pain was noted. This patient is still under observation. The other three operations, done earlier, had entirely satisfactory clinical results from the incomplete sympathectomy.

TABLE VIII RELATION OF RESULT OF SYMPATHECTOMY WITH COMPLETENESS OF DESWEATING

RESULT FROM SYMPATHECTOMY	COMPLETENESS OF DESWEATING (PER CENT OF GROUP TESTED IN EACH CLASS)				
	GRADE I	GRADE II	GRADE III	GRADE IV	TOTAL
	I	II	III	IV	
Class I					
Upper extremity	17	67	16	0	100
Lower extremity	50	0	50	0	100
Class II					
Upper extremity	0	100	0	0	100
Lower extremity	50	25	25	0	100
Class III					
Upper extremity	40	60	0	0	100
Lower extremity	0	100	0	0	100
Class IV					
Upper extremity	0	0	0	0	0
Lower extremity	0	0	100	0	100

Note. 1 In the upper extremity group the 16 per cent of Grade III desweating in the Class I results represents one case.

2 In the lower extremity group the 40 per cent of Grade III desweating in the Class I results, the 25 per cent in the Class II results, and the 100 per cent in the Class IV results represent a total of four cases.

Unfortunately the entire series could not be tested, and the number of cases represented in Table VIII totals only twenty-eight. The series is probably too small to permit any definite conclusions. However, the data as we have them do not show any correlation between the completeness of the sympathectomy as measured by the dermometer and the results in relief of pain (Figs 2, 3, and 4). This is not to be interpreted as indicating that one should be satisfied with anything less than a total denervation of an involved extremity. It is our definite feeling, although we have no proof, that one should always completely denervate the involved extremity if one wishes to get the best results from sympathectomy in the treatment of causalgia. Further, if a patient with true causalgia fails to obtain a satisfactory result following sympathectomy, estimation of the completeness of the operation should be done. The dermometer offers a convenient method. If the sympathectomy is incomplete, reoperation should be considered.

There has been offered, by Mayfield and Devine,<sup>7</sup> an explanation for the possible occurrence of poor results following sympathectomy. They state that

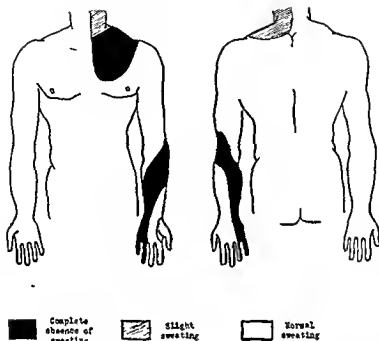


FIG 2—Complete relief of pain (Class I) after incomplete (Grade III) dorsal sympathectomy

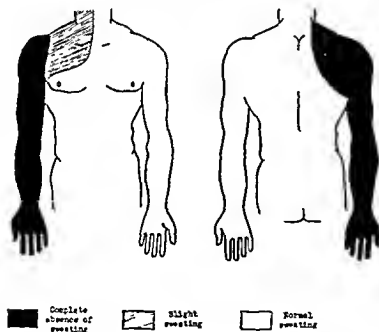


FIG 3—Incomplete relief of pain (Class III) after complete (Grade I) dorsal sympathectomy.

it is necessary to sympathectomize the area of the wound in order to produce the desired effect. Yet, they make three other pertinent assertions: (1) they state that all their patients with lower extremity causalgia had wounds proximal to the knee; (2) they state that their usual procedure is the removal of the second and third lumbar sympathetic ganglia, or the second, third, and fourth, which others agree usually sympathectomizes the lower leg, not the thigh; (3) in their experience all patients except one had satisfactory relief of pain. The conclusion is inescapable that rarely could they have sympathectomized the wound in the case of the lower extremity, and yet rarely did they fail to relieve the pain. It is difficult to believe, in view of this, that failure to denervate the area of the wound is a cause for incomplete or poor relief of causalgia following sympathectomy.

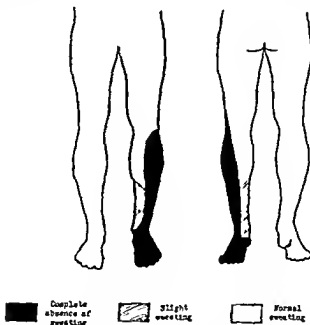


Fig. 4—Complete relief of pain (Class I) after incomplete (Grade III) lumbar sympathectomy.

In summary, from the analysis of our results following sympathectomy, we can find no single factor to which one can point as a cause for some patients obtaining complete relief, and others obtaining only partial relief from this procedure.

#### RESULTS OF RESECTION OF NEUROMA AND GLIOMA

In the group of patients with typical causalgia, there are five cases in which resection of the neuroma and glioma of the involved nerve was performed because at exploration of the nerve the anatomic lesion found demanded resection and end-to-end anastomosis. Four of this group have not had sympathectomy, while the fifth is the previously referred to individual who failed to obtain relief from an incomplete sympathectomy performed prior to nerve

surgery. The five patients all showed typical lower extremity causalgia in the tibial nerve distribution. In the two patients so tested prior to nerve surgery, procaine block of the lumbar sympathetic ganglia gave a good relief of pain for from five to thirty minutes.

In two patients, one of whom had severe causalgia and the other of whom had moderate causalgia, complete relief of pain followed resection of the neuroma and glioma of the sciatic nerve, in a third there was some relief of the burning—enough so that the patient did not require subsequent sympathectomy. The fourth patient had some improvement in the causalgia for six weeks after neurorrhaphy of the sciatic nerve, but following this period the pain returned in its original intensity. He is now under consideration for sympathectomy. The fifth patient, previously mentioned, has had no relief from the tibial neurorrhaphy, and is to have a second sympathectomy through a high, anterior, transverse incision.

This series of cases is very small, and no definite conclusion can be drawn from it. However, together with the experience in World War I<sup>10</sup> that injection of 60 per cent alcohol into the involved nerve at or proximal to the level of the lesion sometimes produced immediate and apparently lasting relief of causalgia, it does suggest that resection of the neuroma and glioma of the involved nerve may on occasions bring about complete relief of pain. Thus, in cases with clinically complete nerve lesions and mild or moderate causalgia in the distribution of this nerve, it is probably wise to explore the nerve lesion first, particularly in the case of the lower extremity. If the lesion found in the nerve itself demands resection, it should be resected. Some patients so treated may be relieved of pain and thus not require sympathectomy. Those who continue to have pain should subsequently be subjected to sympathectomy.

#### SUMMARY AND CONCLUSIONS

- 1 Causalgia is a definite pain syndrome, associated with injury to a peripheral nerve containing sensory fibers.
- 2 The pathogenesis of the syndrome is not known.
- 3 It is not certain that causalgia occurs only in incomplete anatomic lesions.
- 4 The data on fifty-two cases of causalgia and nine of atypical post-traumatic painful states are reviewed. The clinical characteristics of causalgia are enumerated.
- 5 There are cases of post-traumatic painful extremity associated with a lesion of a peripheral nerve which differ from true causalgia to varying extents; occasional cases are distinguished from this syndrome only by their failure to be aggravated by disquieting factors in the individual's environment.
- 6 The pain of causalgia is usually relieved or abolished by adequate sympathectomy. There is no relation between the completeness of the relief and any known factor.
- 7 Resection of the neuroma and glioma of the involved nerve, particularly in the lower extremity, occasionally provides relief of the causalgia.

**NOTE:** Since completion of this manuscript seventeen additional patients with true causalgia were satisfactorily treated by dorsal or lumbar sympathectomy, complete in each instance (Grade 1 or II by dermometer study). Clinical data and results from surgery are parallel to those just described.



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# BENIGN CAVERNOUS HEMANGIOMA OF THE SPLEEN

## LITERATURE REVIEW AND CASE REPORT

O. B. HODGE, M.D., AND DAVID A. WILSON, M.D., DURHAM, N. C.

(From the Department of Surgery, Duke University School of Medicine and Hospital)

**B**ENIGN cavernous hemangioma of the spleen is rare. We have been able to find reports of only thirty-one cases in the literature which appear to us to represent this condition. Malignant lesions of the spleen are much more frequently reported. Smith and Rusk (1923)<sup>1</sup> collected 104 cases of primary malignant lesions of the spleen. Since this time other authors have reported smaller series.

Dowd (1915),<sup>2</sup> Akeakoyunlu (1938),<sup>3</sup> Cole and Forsee (1940),<sup>4</sup> and Pines and Rabinovitch (1942)<sup>5</sup> reported series of thirteen, twenty-one, twenty-three, and forty-two cases of benign cavernous hemangioma taken from the literature. When the cases in these series are thoroughly analyzed, it becomes evident that some do not represent true benign lesions.

Due to the lack of uniformity in classification, many cases labeled benign cavernous hemangiomata are in reality angiosarcoma, angioendothelioma, angioblastoma, simple sinusoid ectasia, etc. Many of the reported cases of benign cavernous hemangioma have been asymptomatic and were incidental autopsy findings. Other cases were surgical and presented a mass in the upper abdomen causing symptoms of pain, or were due to rupture (spontaneous or traumatic) with severe internal hemorrhage.

## CASES IN THE LITERATURE

Hoge (1895)<sup>6</sup> reported the first successful splenectomy performed by McGuire for this condition. Dowd (1915)<sup>2</sup> collected twelve cases of splenic hemangioma from the literature and added one case of his own. Six of these were malignant and had metastases to other organs [Langhans (1879),<sup>7</sup> Homans (1897),<sup>8</sup> Theile (1904),<sup>9</sup> Jores (1908),<sup>10</sup> Ernst (1912),<sup>11</sup> and Dowd<sup>2</sup>]. Of the seven benign cases four were incidental autopsy findings [Albrecht (1902),<sup>12</sup> Theile (1904),<sup>9</sup> and Lubarsch (1905)<sup>13</sup>]. Splenectomy was successful in the remaining three cases [Martin (1909),<sup>14</sup> von Benekendorff (1908),<sup>15</sup> and Anzillotti (1913)<sup>16</sup>]. Steden (1924),<sup>17</sup> Naher (1925),<sup>18</sup> Schwartz (1930),<sup>19</sup> Wassilijeff and Pratasewitch (1930),<sup>20</sup> Zeno and Cid (1930),<sup>21</sup> Kellert (1932),<sup>22</sup> Palavecino and associates (1932),<sup>23</sup> Haines and Mellroy (1933),<sup>24</sup> Grove (1937),<sup>25</sup> Dawson (1937),<sup>26</sup> Schottenfeld and Wolfson (1937),<sup>27</sup> Akeakoyunlu (1938),<sup>3</sup> Nesler, Faber, and Leik (1939),<sup>28</sup> Cole and Forsee (1940),<sup>4</sup> and Stuhlinger (1943)<sup>29</sup> each reported one case treated by splenectomy.

Krumbhaar (1927),<sup>30</sup> Mikami (1933),<sup>31</sup> Goldberg (1940),<sup>32</sup> Aronson and Fox (1940),<sup>33</sup> and Bostiek (1945)<sup>34</sup> each reported one autopsy case. Only three of the six autopsy cases reported by Pines and Rabinovitch (1942)<sup>5</sup> appear to us to represent benign cavernous hemangioma.

## ETIOLOGY AND PATHOLOGY OF SPLENIC NEOPLASMS

In order to bring out the relationship of benign hemangioma to other splenic neoplasms, a brief discussion of the etiology and pathology seems warranted.

The pathogenesis of splenic neoplasms, as with neoplasms in other sites, is not known. However, there are certain factors that may be contributory. Smith and Rusk (1923)<sup>1</sup> in reviewing 104 cases of primary malignant lesions found a history of malaria in 13 per cent, syphilis in 4 per cent, trauma in 4 per cent, tuberculosis in 13 per cent, and typhoid fever occasionally. Secondary neoplasms are much more frequent than primary lesions. Krumbhaar (1927)<sup>20</sup> analyzed 6,500 autopsies from the Philadelphia General Hospital. In this group he found forty cases of splenic neoplasm (1.9 per cent of the tumors). Six were primary and only one represented a benign cavernous hemangioma.

Secondary neoplasms are rare when compared with this condition in other organs. This has been attributed to the absence of afferent lymphatics except for a few in the capsule, the sharp angle of the splenic artery, the pulsating action of the spleen in preventing lodgment of tumor cells, and to an intrinsic antagonistic effect of the spleen toward neoplastic growths. It has been shown experimentally that animals are more susceptible to tumor growth following splenectomy.

The spleen consists of four types of tissue capable of giving rise to neoplasm: the capsular and trabecular framework, the lymphoid element, the reticulo-endothelial, and the vascular elements. The classification of splenic tumors is outlined in Table I.

TABLE I. TYPES OF SPLENIC TISSUE CAPABLE OF GIVING RISE TO NEOPLASM

TISSUE TYPE		BENIGN	MALIGNANT
Capsular and trabecular framework	fibrous, smooth	Fibroma	Fibrosarcoma
	muscle, nervous	Leiomyoma	Leiomyosarcoma
Lymphoid		Neuroma	Neurosarcoma
		Lymphoma	Lymphosarcoma
		----	Endothelioma
Reticuloendothelial			Reticulum-cell sarcoma
			Hemangioendothelioma
			Angiosarcoma
Vascular		Hematoma	
		Lymphangioma	

Ewing<sup>21</sup> stated that endothelioma is the commonest primary type. Mallory,<sup>22</sup> however, believed that the lymphoblastomas are the commonest. MacCallum<sup>23</sup> pointed out that tumors of doubtful origin are likely to be labeled endothelioma. Smith and Rusk<sup>1</sup> in their study of a large series of primary malignancies of the spleen have considered lymphosarcoma to be the commonest malignancy that involves this organ and is usually associated with a generalized process.

The commonest secondary malignant tumor of the spleen is carcinoma (Krumbhaar).<sup>20</sup> Other secondary tumors are melanosis, myeloma, lymphosarcoma, sarcomatosis, and endothelioma.

Cysts of the spleen should be given consideration in a discussion of the neoplastic lesions of this organ. They may be divided into three main types: (1) hemorrhagic cysts which arise from degenerated pulp or from angiomatous

areas. These may later develop into serous cysts. Traumatic subcapsular cysts are usually due to old hematomas and frequently contain cholesterol crystals (2) Dermoid cysts due to epithelial and mesothelial inclusion. These may undergo carcinomatous change. (3) Parasitic cysts

Small involution cysts may be due to trauma or inflammation. They are usually multiple and may be superficial or deep.

Hemangioma is a tumor comprised primarily of new blood vessels, the anlage of which is thought to arise from vascular disarrangement. The process begins by budding of endothelium from a segment of a vessel and results in the formation of new vascular spaces which are either capillary or cavernous in character. To a large extent hemangiomas have a closed vascular system and do not communicate freely with the normal vascular bed. They tend to displace rather than to replace the surrounding parenchyma.

Congenital nevi are thought to be the result of a vascular disarrangement and are not true tumors. They may, however, give rise to hemangioma. The finding of congenital nevi in the spleen should not be considered as constituting a new growth.

In simple sinusoid ectasia there is a free communication of the telangiectasis with the normal vascular spaces. This condition does not fulfill the criteria of hemangiomas.

#### CASE REPORT

M. A. B. (B13507), a 35 year old married colored woman, was admitted to the hospital on July 7, 1943, with a complaint of an upper abdominal mass of four months' duration with rapid increase in size during the previous three weeks.

Past history revealed that she was seen for the first time in the medical clinic twenty months previously. Following examination a diagnosis of syphilis and aortitis was made. At this time the abdominal examination revealed slight epigastric tenderness and the spleen was palpated three fingerbreadths below the costal margin. The patient was referred to the health department for anti-syphilitic therapy.

She did not report for treatment and was again seen two months before admission complaining of an upper abdominal mass of eight weeks' duration associated with pain radiating into the back. Examination disclosed a large mass in the left upper quadrant of the abdomen. It was felt that she had a pancreatic or splenic tumor and hospitalization was advised.

She returned for admission on July 7, 1943. The abdominal mass had increased rapidly in size. There were some digestive disturbances and constipation. During the previous three weeks she had been having an afternoon fever and was bedridden because of abdominal discomfort and pain in the back. On the day before admission she complained of hematuria. There was no history of trauma or malaria.

Examination revealed a temperature of 38.4° C, pulse 100, respirations 30, and blood pressure 160/108. The patient was an obese colored woman who did not appear ill. The abdomen was protuberant (Fig 1, A and B). The lungs were clear. The heart was enlarged to the left and the rate and rhythm were regular. No murmurs were heard.

The abdominal examination revealed a large firm mass occupying the upper abdomen and left flank. It extended into the epigastrium and down to the level of the iliac crest. The mass was slightly movable and appeared to be cystic in the epigastric region. There was moderate tenderness in this area. The liver and kidneys were not palpated. Pelvic examination did not reveal any abnormalities.

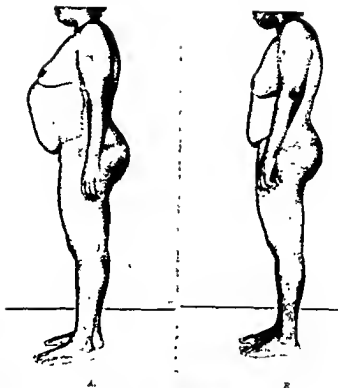


Fig. 1.



Fig 2.

Fig 1—A. Preoperative, note the marked protuberance of the abdomen, the mass was cystic in the epigastrium. B. Patient ten days following operation.

Fig 2.—Roentgenogram of the abdomen showing most of the detail obscured by a large soft tissue mass. The stomach is displaced to the right and the colon downward.

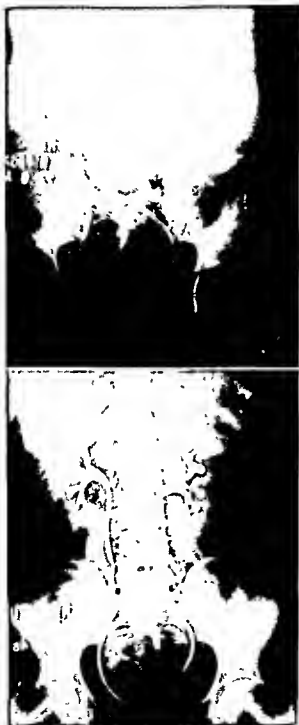


Fig. 3.—Preoperative and postoperative retrograde pyelograms showing displacement of the left kidney and return to a normal position following operation

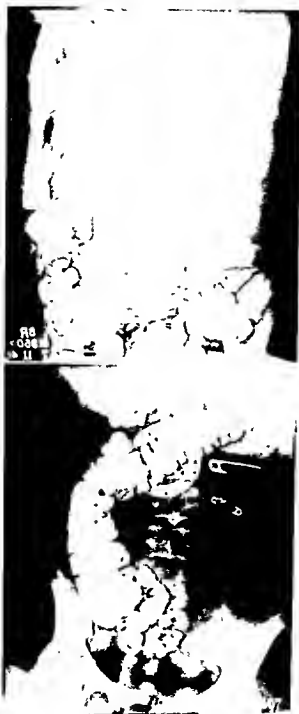


Fig. 4—Preoperative and postoperative gastrointestinal barium studies showing displacement of stomach and colon and their return to a normal position following operation.

Laboratory findings were hemoglobin, 82 per cent; red blood cells, 4,080,000; and white blood cells, 14,000. Differential count showed 41 per cent polymorphonuclears, 41 per cent small lymphocytes, 8 per cent large lymphocytes, 2 per cent eosinophiles, 1 per cent basophiles, 1 per cent stabs, and 3 per cent monocytes. The serology test for syphilis was positive. Total serum proteins were 8.3 Gm. per cent, the albumin being 3.1 Gm. per cent and the globulin 5.2 Gm. per cent. The urine had a trace of albumin on occasions. Kidney function tests were normal and the nonprotein nitrogen was 21 mg. per cent. Stool examination was negative.

Röntgenogram of the abdomen showed most of the abdominal detail obscured by a large upper abdominal soft tissue mass (Fig. 2). Fluoroscopy of the chest revealed elevation and poor movement of the diaphragm. The heart was in a transverse position and there was slight ventricular enlargement.

With retrograde pyelograms the left kidney was found displaced by a mass into the right lower quadrant (Fig. 3). Gastrointestinal series showed the stomach pushed to the right and the colon displaced far downward (Fig. 4). The electrocardiograph revealed sinus nodular tachycardia with left axis deviation and an isoelectric T.

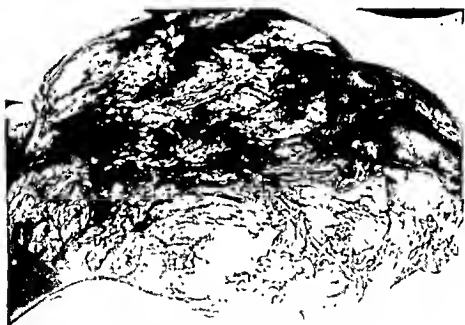


Fig. 5.—The tumor, including the aspirated sanguineous fluid, weighed 13,130 Gm. Approximately 12,000 c.c. of fluid were removed from the cystic mass before extirpation was carried out. The dimensions were 25 by 25 by 30 cm.

On July 12, 1945, the patient was operated upon and a large cystic mass occupying almost three fourths of the abdominal cavity was found. This mass arose from the inferior medial aspect of the spleen which was markedly compressed. Approximately 12,000 c.c. of bloody fluid were aspirated from the cystic mass before removal was carried out. The mass and compressed spleen were inseparable.

On pathologic examination the lesion was found to be a benign cavernous hemangioma arising from the spleen. There was a large cyst associated with the hemangioma. The tumor weighed 13,130 Gm, the largest yet reported, and had a diameter of 28 cm. The patient made an uneventful recovery and was discharged from the hospital on July 23, 1945, eleven days postoperatively. A recent follow up study revealed that she was in good health.





Fig. 6.—Microscopic examination. A. Note the large cavernous and cellular blood spaces lined by endothelium. There are areas of organization and evidence of developing new vascular spaces. B. Sections taken through cyst wall showing relationship to tumor.

## COMMENT

The diagnosis of benign cavernous hemangioma may be extremely difficult. It was an incidental finding in eleven of twelve autopsy cases. In the other case there was rupture of the lesion with death from severe hemorrhage. In the nineteen patients treated surgically, three had spontaneous rupture with serious hemorrhage into the abdominal cavity. (Haines and McIlroy,<sup>24</sup> Nesler, Faber, and Leik,<sup>25</sup> and Cole and Forsee<sup>4</sup>.) A diagnosis of perforated gastric ulcer was made in two and appendicitis in one. The other surgical cases presented the following combination of signs and symptoms: abdominal mass or splenomegaly, pain, dyspnea, dysphagia, gastrointestinal disturbances, and anemia.

Splenic hemangioma should be suspected in patients with splenomegaly unrelated to a general disease process. When rupture (spontaneous or traumatic) occurs, shock, pain, and signs of generalized peritoneal irritation are usually present. Shock must be combated and immediate operation is imperative.

## SUMMARY

We have been able to find only thirty-one cases in the literature that appear to us to represent true benign cavernous hemangioma. Another case is reported. In nineteen of the reported cases in the literature, treatment was by splenectomy. Twelve were autopsy findings.

Some of these lesions may attain an enormous size and undergo cyst formation. In four of the cases there was spontaneous rupture with severe hemorrhage into the abdominal cavity. Thorough microscopic examination of many of the traumatic cysts of the spleen might disclose an underlying hemangiomatous lesion and unless this is kept in mind cases may be missed.

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## CYSTADENOMA OF THE PANCREAS

WITH PRESENTATION OF ONE CASE AND REVIEW OF TWENTY-EIGHT CASES  
COLLECTED FROM THE MEDICAL LITERATURE

RAYMOND E. BENSON, M.D., AND WAYNE GORDON, M.D., BILLINGS, MONT.

(From the Departments of Surgery and Medicine, The Billings Clinic)

**C**YSTADENOMA of the pancreas is a strikingly distinct pathologic entity. It is characterized by slow growth, absence of early symptoms, and later development of a palpable tumor, upper abdominal pain, and weight loss. Occasionally diabetes mellitus is an associated finding. Pathologically it is distinguished as a benign, multilocular, cystic, adenomatous neoplasm which most often originates from the tail or body of the pancreas. That it is an uncommon tumor is evidenced by the fact that there are only about sixty cases reported in the medical literature. The following case illustrates the condition and demonstrates the efficacy of surgical excision.

### CASE REPORT

Mrs. D. M., a white woman, aged 65 years, was examined at the Billings Clinic on March 6, 1945. The chief complaints were upper abdominal pain and weight loss.

The patient was of Italian descent and had come to America from Italy at the age of 18 years. She had had five uneventful pregnancies. The menopause occurred in 1932. There was no known family history of tuberculosis, diabetes, cancer, or other significant diseases. She had had the usual childhood sicknesses but aside from this had been well until December, 1940. At this time the patient first developed pain in the upper abdomen, associated with a moderate loss of weight. It was ascertained at this time that the patient had cholelithiasis and mild diabetes mellitus. In May, 1941, cholecystectomy was performed. The gall bladder contained many large and small stones. The postoperative convalescence from this operation was marred by the development of bronchopneumonia from which she eventually made a complete recovery. The diabetes continued to be mild after this operation and was controlled in the hospital by dietary restrictions alone. After dismissal it became necessary to give her a more liberal diet and ten units of insulin daily.

When seen on March 6, 1945, the patient stated that the complaints for which cholecystectomy had been performed had not been relieved by the operation. In the intervening four years the epigastric and upper abdominal pain had been present constantly. It was intermittently more severe and radiated through to the region of the upper lumbar and lower dorsal spine. The pain had become progressively more intense and for many weeks prior to examination the patient had been confined to bed the majority of the time. Ingestion of food seemed to make the distress somewhat worse. There was no selective dyspepsia. In the four and one half years since the onset of the illness the patient had lost fifty pounds in weight. There was a concomitant loss of strength and general debility. Food ingestion had been slightly restricted.

Physical examination revealed a short stocky woman who showed evidences of severe recent weight loss. The blood pressure was 180 mm. of mercury systolic and 90 mm. of mercury diastolic. The temperature was 98.6° F.; the pulse, 72 per minute. There were upper and lower artificial dentures. A small nodular goiter was palpable but there were no evidences of hyperthyroidism. The heart was moderately enlarged. No murmurs were audible. Auscultation of the lungs revealed a few basal rales. The abdomen was obese. There was an old surgical scar in the right upper quadrant of the abdomen. In the left

upper abdominal quadrant a distinct nodular mass was palpable. It was rounded and approximately 12 to 14 cm. in greatest diameter. The mass moved with respiration and showed considerable mobility in the longitudinal axis of the body. The mass itself was only slightly tender. The point of greatest tenderness was in the epigastrium above and to the right of the umbilicus. Pelvic examination revealed a moderate cystocele and rectocele with associated mild prolapse of the uterus. Rectal examination was not informative. There was no significant deformity of the spine. First percussion over the upper lumbar and lower dorsal vertebrae, and in the left flank area elicited abnormal tenderness. There were mild varicosities of both lower extremities. The tendon reflexes were equal and active.

Erythrocytes numbered 4,900,000 per cubic millimeter, leucocytes, 6,000 per cubic millimeter. Hemoglobin estimation was 17.2 Gm. per 100 c.c. (110 per cent). Urinalyses were essentially negative. The serologic test for syphilis was negative. The blood sedimentation rate was 10 mm. in one hour. The fasting blood sugar was 134 mg. per 100 c.c. The blood urea nitrogen was 14.2 mg. per 100 c.c. Roentgenograms of the colon following the administration of a barium enema revealed normal contours and no evidence of intrinsic disease. Roentgenograms of the stomach following the ingestion of barium were negative. There was no gastric retention. Stereoscopic roentgenograms of the chest revealed no significant abnormalities. Roentgenograms of the dorsal and lumbar spine were not informative except for the presence of minimal changes characteristic of the senescent type of arthritis. Intravenous urograms showed loss of some of the fine renal markings but no significant deviation from the normal.

In view of the noninformative roentgenologic findings it was reasoned preoperatively that the tumefactive intra abdominal lesion was probably situated in the tail of the pancreas. That the spleen or a mesenteric cyst was the site of origin of the tumor was also considered. Operative intervention was advised and accepted. The diabetic state was still mild and no evidence of acidosis had occurred although the patient had neglected dietary care and frequently had had glycosuria before admission to the hospital.

On April 10, 1943, under nitrous oxide, oxygen, and ether anesthesia exploratory laparotomy was performed. The abdomen was opened through a long primary upper left subcostal type of incision dividing the left rectus muscle. Primary exploration of the liver, stomach, duodenum, small and large intestine, and pelvic organs was negative. The gall bladder had been removed previously. In the left upper quadrant bulging through the gastrocolic omentum was a large tumor mass. It displaced the transverse colon slightly downward and the fundus of the stomach upward. The gastrocolic omentum was divided and the tumor exposed. It presented a most unusual appearance. It was about the size of a grapefruit and consisted of many smooth encapsulated grapelike nodulations which varied in color from lime to deep purple. The mass was adherent posteriorly to the splenic vein. It arose from the tail of the pancreas and had replaced this portion of the pancreas and some of the distal portion of the body of the pancreas. The tumor, a segment of the splenic vein, and a distinct cuff of normal pancreatic tissue were then removed in toto. The remaining stump of the pancreas was closed with interrupted sutures of chromic catgut and fine silk. That portion of the pancreas which remained consisted of the entire head and as much of the body as extends approximately 4 cm. to the left of the superior mesenteric artery. At the conclusion of the operation splenectomy was performed and 5 Gm. of sulfathiazole were dusted intraperitoneally. Two Penrose drains were inserted down to the inverted end of the pancreas and the abdomen was closed.

The specimen consisted of a lobulated tumor mass 8.5 by 10 by 5 cm. in diameter. The cut section was multilocular and contained innumerable small cystic cavities, the largest 1.5 cm. in diameter. These spaces were filled with gelatinous fluid which varied in color from amber to deep red and purple. In one portion there was a small cuff of tissue that proved to be, grossly and microscopically, essentially normal pancreatic tissue. The numerous walls of the multilocular cysts were composed of dense fibrous tissue. The cavities were lined with flat cuboidal epithelium. The picture was that of benign cystadenoma of the pancreas. Another portion of the specimen consisted of an essentially normal spleen by gross and microscopic examination.

The convalescence of the patient was marred by the development of a small pancreatic fistula. For several weeks post-operatively a thick fluid escaped from the wound. Four weeks after the operation the patient became quite ill with fever (temperature 103° F.) and considerable abdominal pain. This was occasioned by removal of the drains. Following incision and drainage of a small collection of fluid beneath the original incision the patient progressed rapidly. Eight weeks after the operation the wound had healed completely and the patient was ambulatory and able to attend to some of her usual household duties.

On Dec. 7, 1945, nine months after operation the patient returned for a thorough résumé of her physical status. At this time she was feeling well and had only the minor complaint of slight weakness in the extremities. She had gained twenty pounds in weight and had resumed all her former duties. Abdominal examination was negative. There was no evidence of any mass or tenderness. A glucose tolerance test was performed using the Exton-Rose technique. The fasting blood sugar was 145 mg. per 100 c.c. and the highest blood sugar at the end of one hour was 316 mg. The patient had not been following the diet and had been taking insulin irregularly. She had had no glycosuria before breakfast in spite of the irregular habits. The diabetic state was essentially unchanged by operation.

#### DISCUSSION

*Pathologic Considerations*—Cystadenoma of the pancreas is a true neoplasm composed of multiple cystic cavities lined by cuboidal or columnar epithelium. The cysts contain fluid which may be thin and watery in consistency but which more often is thick and viscid or gelatinous. Sometimes the fluid is light yellow in color but more often, and especially when it is of a viscid consistency, it is dark brown or purple or red, an effect which is said to result from hemorrhage into the spaces (Figs 1 and 2). The cyst fluid is said to contain no ferments.<sup>7</sup> The epithelial lining of the spaces is characteristically low cuboidal or columnar in type, and often there are no papillary infoldings (Fig. 3). When papillary projections are found Dockerty believes that they should be classified as malignant even though the usual microscopic criteria for malignancy are minimal. The recorded experiences of Speese and Young in which such "benign" papillary cystadenomas invaded surrounding structures after incomplete excision or underwent frankly malignant degeneration lend strength to this viewpoint. The more common practice, however, has been to classify these papillary cystadenomas of the pancreas as benign in the absence of direct microscopic evidence of malignancy in spite of their occasional aberrant invasive properties.

In some cysts which grow to very large size, the epithelial lining may be completely destroyed. If smaller spaces are found surrounding the large cyst which continue to retain their epithelial linings, the condition may still be classified as cystadenoma. When none of the fluid-filled cavities are lined with epithelium, the condition is some other than cystadenoma.

Cystadenomas of the pancreas are usually well encapsulated but they may be densely adherent to surrounding structures. Most often they are embedded in and have replaced the pancreatic tissue. Occasionally cystadenomas are pedunculated and attached to the pancreas by only a narrow stalk. The blood supply is usually profuse. Numerous large dilated veins are commonly found coursing over the capsule of the tumor. All variations in size have been observed from small tumors "about the size of a walnut" to very large tumors. Kennard

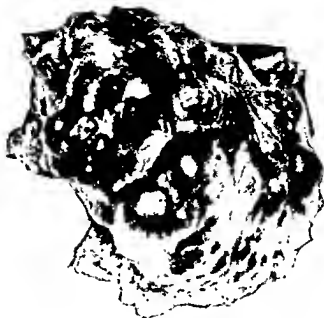


Fig. 1.—Cystadenoma of the pancreas, specimen obtained at operation upon a 63-year-old white woman. The tumor occupied the tail and major portion of the body of the pancreas.



Fig. 2.—Cut surface of the same tumor depicted in Fig. 1. The tumor is composed of many large and small cystic epithelial lined cavities which contain multicolored gelatinous fluid.

reported a case in which the mass measured 15 cm. in diameter and weighed 2,050 Gm. In one of the cases presented by Bowers and associates, the tumor measured 18 by 12 by 13 cm.

The stroma is often composed of narrow connective tissue septa. Sometimes the septa are broad bands in which hyalinized areas may be seen. Smooth muscle fibers may be present in the stroma. The source of these, according to Brunschwig, has been stated as being derived from previously patent vessels and pancreatic ducts. In the case reported by Carling and Hicks, areas of calcification were encountered. Small epithelial lined spaces of microscopic size may be scattered throughout the wider connective tissue septa.

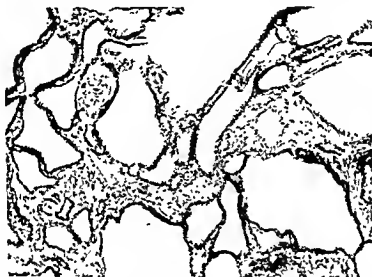


Fig 3—Microphotograph showing the cystic spaces lined with low cuboidal epithelium and no papillary infoldings. The stroma is composed of dense fibrous tissue ( $\times 45$ )

**Clinical Considerations**—Pancreatic cystadenomas occur very infrequently. In 1930, Judd, Mattson, and Mahorner reported that out of 723,397 patients admitted at the Mayo Clinic there were only eighty-eight surgically explored cases of pancreatic cysts of all types. In a subsequent report from the Mayo Clinic by Mahorner and Matson, of 108 cysts of the pancreas only two were found to be cystadenomas. In spite of the rarity of the lesion a review of the literature has enabled us to compile twenty-seven surgically explored cases of cystadenoma of the pancreas. These plus the case herein presented give a series of twenty-eight cases from which to draw conclusions. Many more reports have been perused but because of incomplete data or inconclusive evidence as to the pathologic entity under discussion are not included.

Of the twenty-eight cases, apparently complete removal of the tumor was carried out in twenty-one cases. Incomplete excision was performed in three cases, biopsy alone in three cases, and abdominal exploration with subsequent post-mortem examination in one case. In twenty-six cases in which the result



of operation is known there were eight postoperative deaths (31 per cent). Four of these deaths resulted from abdominal exploration with or without biopsy of the tumor without any attempt being made to remove the growth. In twenty cases in which the tumor was removed and the outcome is known, there were four postoperative deaths (20 per cent). In the fourteen cases cited by Muller in which excision was performed, there were no immediate postoperative deaths, but in three instances death occurred later, possibly associated with the operation. In Brunschwig's series of four cases from the University of Chicago clinics one death occurred. This fatality occurred following radical pancreaticoduodenectomy for an extensive tumor of the head of the pancreas.

The average age of the twenty-eight patients was 48 years. The youngest patient was 17 years of age, the oldest 76. It is thus apparent that the condition is most frequently encountered in the middle age group. Gruber is said, however, to have described two cases occurring in infants. There is a striking disparity in the distribution between the sexes. Of the twenty-eight cases only three (11 per cent) were in males. The greater tendency for women to be affected has been demonstrated previously by Kleinschmidt.

Cystadenomas are most commonly found in the tail and body of the pancreas. In twenty-seven cases of this series in which the situation of the tumor was stated, nine were located in the tail of the pancreas, two involved the body and tail, eight were in the body alone, one arose from the head and body, and seven originated in the head of the pancreas. In Kleinschmidt's review of twenty one cases, two tumors arose in the mid-portion, four involved the entire gland, and the remaining fifteen were in the tail. The fact that the preponderance of these tumors arise in the distal portions of the pancreas (tail and body) has contributed to the good surgical results obtained. It is technically much easier to remove the tail or body of the pancreas than the head.

*The most important clinical finding is a palpable upper abdominal mass.* Of the twenty-seven cases with complete data a palpable tumor was present in all. The mass is most frequently felt above and to the left of the umbilicus in the left hypochondrium. When the tumor is situated in the tail of the pancreas it may sometimes disappear beneath the left costal margin and not be again palpable until the patient assumes the erect position or inspires deeply. Often the tumor is rather freely movable in the longitudinal axis of the body. X-ray studies give no direct information as to the origin of the tumor. Roentgenographic examination of the stomach following the ingestion of barium may reveal a defect in the posterior and inferior aspect of the gastric shadow as a result of extrinsic pressure. Roentgenograms of the colon following the administration of a barium enema may show lateral or downward displacement of the transverse colon or splenic flexure from the pressure of the neoplasm. Urograms are usually not informative except as they eliminate the kidney and adjacent retroperitoneal area as the source of the tumefaction. In the case herein reported, after all manner of x-ray examinations had been performed, there was still considerable doubt preoperatively as to whether or not the palpable tumor

arose from the pancreas or was a plexed spleen or a mesenteric cyst, a dilemma which others reporting this type of case have also encountered

The patient may have no complaints other than the presence of a palpable intra-abdominal tumor, but in the majority of the cases in this series upper abdominal distress or pain was present. In the case herein reported the pain was located in the epigastrium well to the right of the tumor. It was diurnal, severe, and radiated through to the back with such intensity that roentgenographic examination of the spine was undertaken to eliminate the possibility of pathology in the vertebral column. In other cases the pain and distress were much less severe. Dyspeptic symptoms also frequently have been described in association with this type of tumor

It has been adequately demonstrated that the pancreas may harbor a cystadenoma for many years without producing symptoms. Such tumors often grow very slowly and may be symptomless for long periods of time. Brunschwig has recorded the case of a woman, age 62 years, who according to her own statement had been aware of a palpable epigastric mass for ten years. For nine years it had apparently caused no inconvenience. Subsequently, however, she lost thirty pounds in weight and developed diabetes mellitus. At operation a cystadenoma of the head of the pancreas measuring 7 by 4 by 3.5 cm. was removed. With increasing size of the tumor, pain and weight loss ensued. The patient whose record is herein reported lost fifty pounds in weight. Many other examples of subjects who sustained weight losses of thirty, forty, and fifty pounds are available. This weight loss usually occurs in spite of apparently adequate food intake.

Occasionally the first symptoms of a cystadenoma of the pancreas will be those of an acute intra-abdominal catastrophe initiated by hemorrhage from the tumor. A girl, aged 17 years, who had been acutely ill for five days was subjected to emergency laparotomy. At operation the peritoneal cavity was found to contain a large quantity of fresh blood. The source of the hemorrhage was a large cystadenoma of the pancreas. The patient died postoperatively. The post-mortem diagnosis was papillary adenocystoma of the pancreas with hemorrhage.<sup>1</sup> Pettinari's case is also of interest in regard to the association between these tumors and acute abdominal symptoms. His patient, a 70-year-old woman, was suddenly seized with very severe epigastric pain following breakfast of coffee and milk at 9 A. M. That night upon admission to the hospital, emergency laparotomy was performed under the diagnosis of perforated gastric ulcer. The stomach was found to be negative but the pancreas was markedly inflamed and edematous. There were no areas of fat necrosis present. A tumor mass "about the size of a walnut" was found in the region of the neck of the pancreas and was resected with a cuneiform section of pancreatic parenchyma. The abdomen was closed with drainage. A temporary fistula including bile developed and the patient completely recovered. Histologic study of the excised tumor revealed a typical cystadenoma with marked acute leucocytic infiltration of the excised pancreatic parenchyma. Pettinari is of the opinion that there was no causal relationship between the tumor and acute pancreatitis. The latter was assumed to be of "hematogenous origin."

## ANEURYSM OF RENAL ARTERY

### REPORT OF ADDITIONAL CASE

LEONARD V. MARRONE, M.D., UTICA, N. Y.

**A**NEURYSM of the renal artery is, indeed, a rare clinical and pathologic entity. One need only read the excellent review of the literature by Lowsley and Cannon<sup>1</sup> to establish its rarity. In their review of the entire medical literature they found only seventy-four cases. They reported a case of their own (diagnosed preoperatively) making a total of seventy-five cases. Being diagnosed preoperatively, their case makes the twelfth case to be so diagnosed in the "history of the world." Since the excellent presentation by Lowsley and Cannon, however, another case has been reported by Levine;<sup>2</sup> (2) it was diagnosed preoperatively and successful operation was done.

It is the purpose of this paper to present another case of aneurysm of the renal artery diagnosed preoperatively, thus bringing the total to seventy-seven reported cases, fourteen of which were diagnosed preoperatively. The etiology, pathology, signs, and symptoms, so well presented in these references need not be included here.

#### CASE REPORT

B. G., aged 44 years, was seen for the first time Nov. 1, 1943, complaining of pain in the right flank and right upper quadrant for the last three years. At times pain was accompanied by considerable gaseous eructations not related to food intake or type of food, although fatty foods were voluntarily avoided. In the last several weeks the pain had become more constant and severe. There was no nausea or vomiting. Bowel movements were regular and of normal color. There were no associated genitourinary complaints.

Past history was essentially negative except for a repair of an umbilical hernia eighteen years before, and the uneventful births of nine healthy infants. Review of systems was otherwise entirely negative.

Physical examination revealed a short, obese white woman appearing in good health. The abdomen was obese and pendulous. A four inch well healed vertical cicatrix was present just to the right of the umbilicus. The abdomen was soft throughout and no masses or soft organs were palpable. There was slight but persistent costovertebral tenderness on the right side. Pelvic and rectal examinations were negative. The blood pressure was 160 systolic, and 88 diastolic. Laboratory work up, including a Wassermann test, was negative except for a trace of albumin and 8 to 10 white blood cells in the urine.

Röntgenograms were made of the gall bladder and kidneys. The gall bladder functioned normally. The roentgenograms showed a wreathlike calcified shadow lying outside the well outlined gall bladder. Intravenous pyelograms revealed this wreathlike shadow to be lying outside of and medial to the right kidney. Both kidneys functioned normally. A diagnosis of aneurysm of the right renal artery was made.

When the seriousness of this condition was explained to the patient, she readily consented to operative treatment. She was admitted to St. Elizabeth Hospital and on November 7, under general anesthesia, the right kidney and pedicle were exposed through the usual lumbar approach. The pedicle was carefully mobilized and examination revealed a pulsating mass in the hilus of the right kidney.

The preoperative diagnosis having been absolutely substantiated, the kidney was removed in the usual manner, reparative operation being out of the question. The wound healed per primam and the convalescence was uneventful. She was allowed out of bed early with no ill effects and was discharged twelve days postoperatively. Since the nephrectomy she has been free of symptoms.

*Description of Specimen.*—Grossly the kidney appeared normal in every respect. At the bifurcation of the renal artery on the posterior aspect, there was a sacular arterial dilatation. It was reddish yellow in color, firm to touch, and measured 2 by 1.5 by 1.5 cm. The wall of the sac contained calcified plaques. The ant surface of the kidney was normal; the pelvis and calices were not dilated. Microscopic examination of the wall of the sac revealed it to be a true aneurysm.



Fig 1—Surgical specimen showing probe in aneurysm

#### SUMMARY

An additional case of true aneurysm of the renal artery is reported. This makes the seventy-seventh case reported, and the fourteenth case diagnosed preoperatively. A nephrectomy was performed through the usual lumbar approach, and the patient was entirely relieved of all symptoms.

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# CLOSTRIDIAL WOUND INFECTIONS AND GAS GANGRENE

## ARTERIAL DAMAGE AS A MODIFYING FACTOR

LIEUTENANT COLONEL JOHN PAUL NORTH, MEDICAL CORPS,  
ARMY OF THE UNITED STATES

ONLY during time of war is the surgical profession properly conscious of the importance of gas gangrene and allied infections by the anaerobic clostridial organisms. The surgeons who returned from France at the close of World War I had abundant experience with it and most of them remained alert to its frequent occurrence in civilian surgical practice. For a younger generation of surgeons, World War II provided a similar experience and, it is hoped, a continued awareness of its seriousness, for indeed there is no condition in which a high index of suspicion and a prompt diagnosis have greater influence upon the outcome. The loss of life and limb which results from delays is a challenge which can be met only by maintaining constant rather than sporadic interest in this disease. Its occurrence in peacetime, vehicular and industrial accidents, as well as in association with senile or diabetic gangrene, is sufficiently common to warrant such continued attention. Here distinction is being made between clostridial wound infections, which are more or less localized processes having a hopeful prognosis under conservative surgical management, and gas gangrene, which is a diffuse disease carrying an immediate threat to life and urgently demanding radical surgery. This distinction has not always been clearly preserved. The course which a given case will follow is determined not so much by the nature of the invading organisms nor the particular tissues which they invade as it is by the state of adequacy of the arterial circulation. Vascular damage with incompetency thus becomes a very important consideration in prognosis and treatment of all cases of clostridial infection.

### INCIDENCE

Advances in military surgery, notably early débridement of the wound, widespread use of the sulfonamides and of blood transfusion, and air evacuation of the wounded, resulted in a remarkable reduction during World War II in the incidence of anaerobic infection of wounds. The medical history of World War I, issued by the Surgeon General of the Army, recorded that battle wounds involving soft tissues only were complicated by gas gangrene in 10.8 per 1,000 cases, while those wounds which were associated with compound fractures showed this complication in 63 cases per 1,000. The complete figures for World War II are not available, but isolated reports from various theaters of operation are significant. Cutler and Sandusky's report of infection of this type in 18 per 1,000 wounds received in aerial combat is typical and is unusually interesting because of its bearing upon the concept of the essentiality of soil contamination as an etiologic factor. Jeffrey and Thompson reported that the British forces involved

in the Italian campaign had gas gangrene in 10 per 1,000 casualties. Neal and Cole set the incidence at 15 per 1,000 among the casualties on a hospital ship supporting amphibious operations in the South Pacific. Langley and Winkelstein report 16 per 1,000 from an American Evacuation Hospital in Northern France. The cases of perfringens infection which form the material for this paper represent 15 per 1,000 of the battle casualties admitted to a general hospital behind the North Burma front. As will be indicated presently, only one-half of these were true gas gangrene. An analysis of the incidence of gas gangrene in these battle casualty cases, therefore, using the criteria quoted from the Surgeon General's report on World War I, is 6 per 1,000 in wounds involving soft tissues only, and 17 per 1,000 for those with associated compound fracture.

A brief note of the type of work done in this hospital will be helpful in the interpretation of what follows. Situated from 75 to 200 air miles behind an advancing front, the casualties from both American and Chinese ground forces were received by air evacuation. Combat occurred in jungle terrain with heavy soil contamination because of poor hygiene among natives and Chinese troops. The wounded were transported by litter bearers to a portable surgical hospital, set up close to the fighting front and adjacent to a rice paddy or other cleared area where liaison planes of the Piper Cub type could land and evacuate the wounded to larger fields accommodating transport (C-47) planes. From this point there was a one to two hours' flight and a seven-mile ambulance trip to this hospital. Despite the difficulties, evacuation was accomplished with extraordinary rapidity. The average time elapsed between wounding and admission to this general hospital was approximately two days. For the most part, the evacuation hospitals played no part in this chain of evacuation. Often, as might be expected, the tactical situation, lack of landing strips for planes, or extraordinarily thick weather caused delays in air evacuation. The importance of early surgical débridement is emphasized strikingly by the fact that the most severe cases in the entire series occurred in one combat unit which for ten days was cut off from any surgical care other than the limited facilities of their own battalion aid station. It is of some interest to note in passing that the etiologic factor of spore contamination of woolen clothing did not exist, since only cotton was worn in the jungle.

In this report has been included every patient admitted to the hospital over a two-year period who exhibited clinical manifestations of infection by the anaerobic gas-forming organisms. The clinical diagnosis was supported by bacteriologic findings in every case. It should be emphasized that, in approximately one-half the cases under consideration, infection was confined to the region immediately adjacent to the wound, and therefore these cases were not true gas gangrene. Cases have not been included in which clostridia were an incidental finding, but only those with clinical manifestations of acute infection. Had laboratory facilities permitted routine culturing of all wounds, there is no doubt that many more would have been found to harbor these ubiquitous organisms. For example, they were found in an abscess about a shell fragment in the lung and on several occasions about foreign bodies in the brain. There

was no indication in these cases that the presence of clostridia was of clinical significance despite the recent Russian report which indicates that they may, in certain instances, produce serious and even fatal encephalitis. No pathogenic gas-forming anaerobes other than those of the *Clostridium welchii* group were encountered.

#### CONTRIBUTING ETIOLOGIC FACTORS

The factor of greatest importance in influencing the course of the infection seems to be the integrity of the principal arterial trunk of the injured extremity. When this is intact, the infection can be expected to remain localized. However, when there is damage to the brachial or femoral arteries or to both branches below their bifurcation, gas gangrene will probably supervene. The bearing of this observation upon prognosis and surgical management will be discussed presently. It is indeed surprising that in the past attention has been concentrated upon the infectious aspects of the condition to the neglect of this vascular element. It would be thought that the term gangrene alone would have preserved a proper focus. The Surgeon General's *United States History of the World War* does so, and this report contains one of the best descriptions of the pathology of gas gangrene which has ever appeared and is a source of information on the subject which has been too generally overlooked. It states, in effect, that anaerobic bacteria are incapable of producing gas gangrene by their presence alone and must be accompanied by, first, the failure of circulation; second, extensive cellular damage to large quantities of muscle under conditions that prevent free access of oxygen; and third, a constantly progressive increase of this series of factors. These conditions are fulfilled only when there has been damage to a major arterial channel. In thirty-two cases of gas gangrene of an extremity, dissection of the amputated limb disclosed injury to the main arterial trunk in sixteen. In nine additional patients who had had amputations prior to admission, the field record indicated that severe vascular injury was responsible for their gas gangrene. Had the amputated limbs of the seven patients remaining been carefully dissected, we are confident that vascular injury would have been found. Thus, in the gas gangrene cases, certainly 72 per cent, and probably 100 per cent, had major vascular damage. The thirty-seven patients in whom infection remained localized to the region of the wound provide a contrast in that only three (8 per cent) had vascular damage, and this was limited in its extent. One had embolism of the popliteal and two had severance of the anterior tibial artery alone. The course of the disease is so altered by a background of major arterial damage that this feature would seem a more rational basis for classification than the currently popular use of the terms anaerobic cellulitis and anaerobic myositis which are misleading as well as inaccurate. Cellulitis suggests diffuse infection of the superficial tissue planes, whereas it is well recognized that the layer of devitalized muscle is the favored medium for the proliferation of the clostridial anaerobe. Practically speaking, therefore, all cases of clostridial infection can be described as myositis, but the integrity of the circulation of the part is of far greater significance than the depth of the involvement.

The usual arterial damage in battle casualties is a laceration, severance or thrombosis of the vessel due to the missile itself or its explosive force in the tissues. Excessive tension within the tissues may also produce an inadequate circulation. Thus, the compression of a swollen limb by a snug-fitting plaster cast may cut off circulation. The same effect may be obtained by increasing edema within an unyielding muscle sheath, or by progression of a confined hematoma. In civilian practice the factor of arteriosclerosis, either senile or diabetic, must be given consideration.

The influence of soil contamination has already been noted, but these organisms are so ubiquitous that soil is only one of many sources of infection. It was of some interest to note that during the first nine months that this hospital was in operation, not a single case of clostridial infection was observed among a large number of patients treated for crushing injuries and compound fractures resulting from vehicular injuries. During this period, the hospital was serving American supply and Chinese combat troops in training. Later, when the same troops moved into Burma, these infections appeared with regularity. This cannot be explained except on a basis of poorer sanitary conditions in the forward areas. Nor can the fact be explained, except perhaps on the basis of an acquired racial immunity, that the incidence of clostridial infection in American casualties was twice that in Chinese casualties. All except five of the cases considered were associated with battle wounds. Of the exceptions, three occurred in injuries sustained in truck or tractor accidents, one was in a knife wound with severance of the anterior tibial artery, incurred while cutting bamboo, and one was the result of a TNT explosion with extensive thromboses. There were associated compound fractures in thirty-two (46 per cent) of the sixty-nine cases observed. Extensive necrotized soft tissue was noted in most cases, indicating that the débridement had been incomplete, but there was an occasional exception to this rule.

#### DIAGNOSIS

In any serious wound, careful investigation should be made into the adequacy of the arterial circulation. The history of the injury and its location are often more significant than abnormal physical findings. Any evidence indicating that a main arterial trunk may be damaged should put the surgeon on the alert to watch hourly for the onset of gangrene and to act accordingly. This was learned by sad experience when three patients in whom vascular damage had not been suspected developed gangrene in the wards. Several precious hours were lost before amputation and these patients died. Two other patients presented an extensive and hopeless gas gangrene on admission and it was obvious upon reviewing the records that arterial injury was present, but its significance was overlooked by previous attendants. There were, on the other hand, eleven patients whose circulation was recognized as being in a precarious state upon admission. These were all watched very closely and recovery in each instance followed amputation performed at the first evidence of gangrene.

It should rarely be difficult to detect clostridial infection if the surgeon is alert to its possibility. The first four days after injury are the critical ones and



the diagnosis was made within this period in 75 per cent of the cases. A careful direct examination of the wound seldom leaves any doubt in the mind of the experienced surgeon concerning the presence of an anaerobic gas-forming infection. The pulse and temperature chart cannot be relied upon. The laboratory affords methods of bacterial confirmation by smear, but time cannot be lost in awaiting the results of cultures. Sudden increase in pain in the wounded part is a warning signal which requires careful inspection of the wound. As the dressings are removed, the diagnosis may frequently be made by the detection of a "dead house" odor. It is characteristic and unmistakable and is more readily observed at a slight distance than by sniffing directly over the wound. In the early stages, marked edema, tension in the tissues, and a thin serosanguineous discharge may be the only visible signs. Later, crepitation is present in the tissues and also a mottling of the skin with bleb formation. The depths of the wound reveal discolored necrotic muscle, and gas escapes as sealed cavities or tissue planes are opened. Subcutaneous emphysema may be encountered sometimes in wounds of the chest wall or neck, where atmospheric air is trapped under the skin. This should not lead to a mistaken diagnosis, since the typical signs of a clostridial infection are absent from these cases.

No other infection progresses as rapidly as a fulminating case of gas gangrene. It may advance perceptibly in the course of one-half hour. The earliest case in this series was one in which the diagnosis was made twelve hours after the injury and the soldier was dead eighteen hours later. On the other hand, infection may smolder in a wound for days and suddenly light up. One such patient was under careful observation because he had gangrene although no apparent infection of the foot. Refrigeration therapy was tried during this period, in the hope of avoiding above-knee amputation, but on the twenty-second day gas was detected and thigh amputation was necessary. Experience with refrigeration was very limited due to lack of ice, but no effects were observed from it other than the dubious benefit of delaying the onset of clostridial infections.

Delays in the recognition of gas gangrene occurred in all the echelons through which these patients passed. The record is far from perfect. The first case encountered developed in the wards of this hospital. The wound was concealed by a thoracobrachial cast and suspicious of the seriousness of the condition were further dulled by the fact that an associated malarial fever was brought under control by atabrin. It was customary for the patients to arrive encased in plaster casts and there were one or two experiences of this sort of discovering clostridial infection unexpectedly at the removal of the cast. Therefore, an invariable rule was made that the cast must be removed immediately upon admission whenever there was a history which suggested injury to a main artery, whenever there was any evidence whatsoever of circulatory embarrassment, or whenever there was the slightest suspicion that clostridial infection might exist. Continued surveillance of such cases is essential to avoid disaster. On one occasion a nurse on duty at night reported that one of the patients was experiencing unusually severe pain in the wound and that the toes appeared to be dusky. The ward officer had inspected this wound just before he retired and the sig-

nificance of these observations did not impress him. Seven hours later gangrene had extended to the thigh and, although amputation was done, it did not avert a fatality. It is, of course, easier to be wise in retrospect than to be consistent in making the right decision at the time. However, honest criticism of results is good for the soul and helpful in the future. A review of the records of thirty-two cases of gas gangrene leads to the conclusion that, had the diagnosis been as prompt and the surgery as adequate as it might have been, the mortality rate could have been reduced from its actual level of 31.3 per cent to a figure in the vicinity of 20 per cent.

#### SURGERY IN GANGRENE

No delay can be countenanced in resorting to appropriate surgery as soon as a surgeon is satisfied that he is dealing with clostridial gangrene. Appropriate surgery implies amputation. An extremity which is gangrenous is dead and cannot be salvaged. It beclouds the issue to talk of resecting muscle groups. The cases wherein such a limited procedure has been successful were not true gas gangrene within my concept of the term. They were localized clostridial infections. A patient with true clostridial gangrene cannot be made a better risk for operation by resuscitative or supportive measures. These are needed but should be carried out coincidentally with the operation rather than in preparation for it. A patient with gas gangrene does not improve while waiting for the surgeon's knife and not one has been saved without amputation. There are a few patients who seem to be beyond hope of salvage, but even in an apparently moribund patient the desperate gamble which major amputation often involves should be taken. This seemingly radical viewpoint is the product of experience during the early stages of which three patients were regarded as too advanced for radical surgery. Multiple incisions were made in one of these and the other two were not operated upon at all. All three continued relentlessly to a fatal termination within a few hours. Subsequently, recovery followed prompt amputation in at least two patients whose condition on admission appeared to be equally hopeless. The futility of expecting improvement under preoperative supportive measures was driven home by another experience. A patient seriously ill with gas gangrene was given a transfusion and developed a severe reaction. The operation was accordingly postponed and intensive supportive therapy instituted. The gangrene and the toxemia progressed relentlessly. As a last resort amputation was performed after thirty-six hours, but by that time the patient's scant chances for survival had been sacrificed.

Amputations for gas gangrene should be done at a level with good blood supply. This will not coincide with the upper limits of crepitation in the tissues nor even with the furthestmost extent of infection. Recovery has been witnessed after amputation below the shoulder even though subcutaneous emphysema had infiltrated the pectoral region. Patients have been seen repeatedly who did well despite the persistence for many days after amputation of crepitation and of infection in the stump. These cases can be satisfactorily managed as localized clostridial infections provided the circulation of the part is adequate. A limited

experience with hip and shoulder joint disarticulations has not shown that they have any advantages to compensate for the additional operative shock involved and the additional tissue planes which they lay open to infection. The three requirements of amputation in clostridial gangrene are that it be done through a level which ensures vascularity, that it be of the stepped-guillotine type, and that it be left wide open without sutures. In this series of thirty-two patients with gas gangrene, three had no amputation, ten had amputations at the portable surgical units, and nineteen had operations performed in this hospital.

#### SURGERY IN LOCALIZED INFECTION

In the cases where the infection is localized and there is an adequate circulation in the extremity as a whole, it is not necessary to sacrifice the limb. There is not the same desperate urgency about immediate operation as there is for gangrene, but nevertheless there should not be undue delay. My experience included thirty-seven of these cases, none of which progressed to gangrene. Thirty-six of the cases involved an extremity and all patients recovered without loss of the limb. The one case which terminated fatally was a clostridial infection which involved the abdominal wall too extensively for surgical excision. Death from toxemia resulted within twelve hours of this soldier's admission to hospital. In these wounds the organisms proliferate and infection disseminates throughout devitalized tissue under anaerobic conditions. The rationale of surgical intervention is to modify these conditions by the excision of necrotic tissue and the exposure of closed cavities to the air. It is not always possible to remove all the dead tissue at the time of operation and some of the excision may be left for secondary dressings, but it is important that all fascial planes be laid open so that no sealed-off pockets remain. The subsequent dressings of these wounds are major surgical procedures which must be carried out at least once a day. All necrotic tissue must be trimmed away painstakingly until clean granulations cover the surfaces. During this period the oxidizing agents such as zinc peroxide, hydrogen peroxide, ehlorazene, and potassium permanganate all have a useful function in supplementing by chemical means the basic objectives of the surgical wound excision. Somewhat later after the slough has been separated, local application of penicillin seems to be helpful in preparing the surface for skin grafting or suture.

#### ADJUNCTS TO OPERATION

The replacement by transfusion of blood loss which occurred at the time of original injury and during operation is urgently needed in all cases. It constitutes a most important aspect of treatment. Plasma is of value in restoring depleted proteins, but is not a substitute for whole blood in these patients. All will require large amounts of blood on the operating table and during the early postoperative period. The war has taught us to think in terms of gallons rather than pints of blood. This obvious need for transfusion strictly as replacement therapy renders academic any discussion of its value in combating toxemia, although its advantage from this standpoint may also be argued. It has never been shown conclusively that the sulfonamide drugs possess specific affinity

against the clostridial organisms in man. However, the infection of these wounds is invariably a mixed one and among the secondary invaders sulfonamide-sensitive streptococci are common and become important after the clostridial infection has burned itself out. Accordingly, it is sound therapy to institute sulfonamide therapy early in order to build up an effective blood level at a period when it becomes essential.

Experience with the use of *perfringens* antitoxin had been very limited prior to the war. Some of us cherished the belief that greater benefit might have been apparent had it been administered in larger dosage than customarily. Consequently, in the earlier cases the available supply of antitoxin was drawn upon liberally for the American patients, giving usually 13,000 units every six hours. There were thirteen patients who received a total dosage of 100,000 units or more, with a maximum dosage of 208,000 units. Since the antitoxin was not available for administration to Chinese patients, there was a parallel series of controls. Midway in the series stock was taken and it was impossible to discover that any advantage had accrued from the use of antitoxin. Thereafter, antitoxin was given only to an occasional patient and, in reviewing the series carefully, no reason could be found to regret this deliberate omission.

Enthusiastic reports have appeared concerning the value of penicillin in the therapy of these cases, particularly its prophylactic benefit when given in large dosage in the forward installations soon after wounding and before definitive surgery could be done. I agree with Cutler and Sandusky and with Jeffrey and Thompson that it must be considered only as an adjunct to early and adequate surgical intervention, although the experience does not provide data for a sound assessment of its value. In the early phases of the Burma campaign, penicillin was not available and it was during this period that most of the cases of frank gas gangrene were encountered. Later, when the drug was available in liberal amounts, evacuation of the wounded from the front had been accelerated, earlier errors in the use of constricting plaster casts had been corrected, and there was an alertness to the possibilities of clostridial infection throughout all echelons. A considerable number of cases were seen of localized clostridial infection during this period, but, as has been shown, this group has virtually no inherent mortality risk, and relative morbidity is difficult to prove statistically. Thus we have recourse only to personal impressions of the benefit accruing in six patients with true gas gangrene. One of these had had amputation before admission and died within twelve hours. A second had amputation as soon as gangrene was detected on the third day after injury. He received one-half million units of penicillin without appreciable effect upon the downhill course. The other four patients recovered but in three of them this might have been predicted because the presence of gas gangrene was recognized and amputation done within forty-eight hours of wounding. In the final case, the patient was admitted four days after receiving the wound. He had had several incomplete débridements in the forward hospital and the gangrenous thigh was amputated promptly upon admission to this hospital. Postoperatively he received two million units of penicillin and this may well have been a factor in determin-

ing the outcome. It is, however, the only case of gas gangrene in which penicillin appeared to have had significant influence.

Of the group which localized clostridial infections, twenty patients received penicillin in total dosages varying from 600,000 up to five million units. No penicillin was given in seventeen cases which, therefore, represent a comparable control group. None of these localized cases progressed to gangrene and all had the same type of conservative surgery. There were no observable differences in the course of the penicillin-treated cases from that of the controls except for its obvious value in controlling infection due to associated organisms

#### SUMMARY AND CONCLUSIONS

1. Experience with the treatment of clostridial wound infections occurring among Chinese and American troops in North Burma emphasizes the importance of differentiating between those with major vascular damage and those without such injury.

2. Gas gangrene is unlikely to develop unless the integrity of the main arterial blood supply is impaired either by the initial trauma or, secondarily, by such factors as tension within closed tissue compartments or external constriction by improperly applied plaster casts

3. There were in this series thirty-two cases of true gas gangrene, representing an incidence among combat wounded of seven cases per 1,000 casualties. The mortality in this group was 31.3 per cent, and there were none who survived without a major amputation. Neither delay in resorting to surgery nor conservatism in its performance can be countenanced in dealing with this condition. A stepped-guillotine amputation through a level of good blood supply without suture of the stump constitutes the indicated surgery.

4. The cases of wound infection by clostridial organisms in which the main blood supply of the part remains intact present an entirely different problem and a much more favorable prognosis. In thirty-seven such patients, none developed gas gangrene, none required amputation, and only one (with an extensive involvement of the abdominal wall) died. Limited surgical excisions which eliminate anaerobic conditions from the wound are adequate for this type of case.

5. All other measures are subordinate to timely and adequate surgery. Blood replacement therapy by massive transfusions is imperative. The sulfonamide drugs are useful although probably not specific. The use of perfringens antitoxin has proved disappointing in practice. Our data do not provide a good basis for evaluating penicillin in these infections, but its use as an adjunct to surgery is advocated.

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# PENICILLIN IN TREATMENT OF CRANIOCEREBRAL INJURIES OF WAR

WITH PARTICULAR REFERENCE TO ITS INTRAVENTRICULAR USE

MAJOR KENNETH H. ABBOTT,\* MEDICAL CORPS,  
ARMY OF THE UNITED STATES

THE high incidence of infections consequent to open (compound) cranio-cerebral and spinal injuries of war has demanded the use of every therapeutic agent and technique known to medical science. In World War II the Army Medical Department made available all of these agents and in particular it has been the good fortune of the Medical Corps to have large supplies of the newest of these, penicillin, in forward installations where definitive care could also be rendered to the injured soldier. It has been my opportunity to study the action of penicillin in more than 250 cases of acute cranio-cerebral and spinal cord injuries. These patients were observed for the most part in evacuation hospitals, and a few were seen in general hospitals, in the Southwest Pacific Theater of Operations. The details of these experiences have been recorded elsewhere.<sup>1</sup>

Because of the comparative innocuousness of penicillin sodium, together with its apparent great prophylactic and therapeutic efficacy in treatment of intracranial wounds, I wish here to record briefly a few observations on the use of this antibiotic agent in sixty-two cases of severe open (compound) cranio-cerebral injuries. Particular mention will be made of the intraventricular application of penicillin, emphasizing its prophylactic value and the absence of toxic or irritative reactions even when it is used in large doses.

One of my first experiences with penicillin sodium in treatment of cranial injuries came with the successful treatment of a soldier who had severe pneumococci (type XXXII) meningitis subsequent to a basal cranial fracture.<sup>2</sup> The observations made on this patient and on subsequent patients whose meningitis was treated intracisternally and intrathecally with penicillin disclosed that the inflamed leptomeninges, and probably the ventricles also, tolerate heavy concentrations of penicillin in the cerebrospinal fluid. When untoward effects did occur they were mild and transitory, as was noted in the foregoing case, in which 100,000 units of penicillin sodium were introduced into the basilar cistern. It was, therefore, planned to administer penicillin routinely by the intracranial (intracerebral, intraventricular, intracisternal, or intrathecal) route in all cases of cranio-cerebral injuries in the ensuing Philippine campaigns in which I participated.

## MATERIAL

Observations were made on the use of penicillin in more than 200 cases of acute cranial injuries of all types. In this group there were sixty-two cases of

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\*Now returned to civilian status, Rochester, Minn.

<sup>1</sup>The untoward effects consisted of nausea, headache, increased respiration, slowing of the pulse, and a temperature of 103° F.

severe open (compound) craniocerebral wounds in which operative intervention was performed and penicillin was administered locally. In all of these cases there were contusions and lacerations of the brain consequent to indriven bone metallic fragments, or bullets. In nineteen instances either bony fragments metallic fragments, or both had entered or perforated one or more ventricles.

The Medical Corps was fortunate in the Philippine campaigns to receive the patients who had cranial wounds at evacuation hospitals within a relatively short time following injury, usually within two to twelve hours, but occasionally as late as three days. These patients had received only minimal treatment in the forward echelons, consisting of a field dressing, plasma, and occasionally also morphine tartrate. Seldom had ill advised surgical treatment been attempted.

#### PLAN OF TREATMENT

All patients who had cranial injuries were admitted directly from the incoming ambulances to the "shock tent," where their first examinations and treatment were begun. The routine treatment consisted of 2 units of double strength plasma,\* followed by 100 cc of a 5 per cent solution of sulfadiazine sodium and 50,000 units of penicillin sodium (dissolved in 10 cc of isotonic saline solution), all given intravenously. Frequently it was necessary to administer from 500 to 1,500 cc of whole blood because of the acute loss of blood consequent to the craniocerebral injury or other wounds. As soon as the patient's condition would permit surgical intervention, he was taken to the operating room and surgical treatment was instituted.

Operation was performed with the patient under one of three types of anesthesia: local (infiltration with procaine hydrochloride and block anesthesia), combined local and intravenous anesthesia (pentothal sodium), or ether-oxygen anesthesia (intratracheal, closed type).

Penicillin was placed intracranially in all wounds according to the following plan. If the brain was lacerated so that a ventricle was found to have been exposed or the foreign body entering the brain had traversed the ventricle, then 25,000 to 50,000 units of penicillin sodium dissolved in 5 cc of isotonic saline solution were introduced into the affected ventricle at the time it was surgically explored. If, however, a small missile had perforated a ventricle and lodged elsewhere and the damage in the cerebral tissue consequent to this was so small that open (visual) exploration of the ventricle was not considered advisable because of the increased trauma incurred by such operative intervention, then penicillin was injected into the ventricle through a ventricular cannula or a small catheter introduced along the track of the missile. Other deep cerebral wounds received 50,000 units of penicillin dissolved in 5 cc of isotonic saline solution directed into the wound, while more superficial wounds received a similar amount placed underneath the dura after its closure had been accomplished.<sup>†</sup>

Penicillin was also used in the scalp wound to irrigate the wound (250 units per cubic centimeter) and also after débridement and closure of the scalp

\*Two units of plasma dissolved in 250 cc of isotonic saline solution  
<sup>†</sup>In all instances the dura mater was closed, either by pr (temporal or fascial lata) or with fascial grafts. If fibrin film was not available.

(10,000 units). Powdered penicillin (crystals) was occasionally sprinkled on uncovered areas of epicranium when there was excessive loss of scalp tissue but was not used as such intracranially. As the calcium salt of penicillin was not available I have not had any experience with its intracranial use such as has been reported by Cairns and his associates.<sup>2</sup>

I was not favorably impressed by the results of my earlier intracranial use of sulfonamides, hence, local sulfonamide therapy was not used in this series of craniocebral injuries.

The postoperative treatment included either oral or intravenous administration of sulfadiazine, in sufficient doses to maintain a concentration of 10 to 15 mg. per 100 cc. of blood and parenteral administration of penicillin. The latter was given intramuscularly in doses of 25,000 units every three hours as routine therapy. This treatment was continued for five to seven days. A few patients received from one to four intracisternal (cisterna magna) injections of 25,000 to 50,000 units of penicillin sodium in 5 cc. of isotonic saline solution each, no patient received more than one injection a day.

#### CLINICAL OBSERVATIONS

It was not possible to follow these patients for a period sufficient to warrant the drawing of any definite conclusions about the incidence of infection and therapeutic efficiency of penicillin, for they were observed only from five to seventeen days in the evacuation hospitals. However, follow-up reports were received from many of them as late as three months after injury and personal follow-up was continued on a few to general hospitals; they were thus observed for thirty to sixty days. So far as I was able to determine there were no post-operative intracranial infections in any of these sixty-two cases. One patient, however, a Filipino boy, whose wound was eighteen hours old at the time he received definitive treatment, did have an infection of the scalp after two weeks. This was traceable to improper handling of the wound after he was transferred to a civilian hospital.

The anesthetists and I observed all of these patients closely at the time when penicillin was introduced into the brain. Particular attention was given to those who received penicillin by the intraventricular route. These observations failed to reveal any untoward effects following the local injection of penicillin into the brain, ventricles, and intracranial subarachnoid spaces at the time of the operation or subsequent thereto. Particular attention was paid to the pulse, respirations, blood pressure, occurrence of vomiting, and condition of the skin. If the patient was conscious, his state of consciousness was closely observed. At no time could we detect any evidence of a toxic or irritative reaction which could be attributed to the penicillin.

The innocuous nature of penicillin was forcefully brought to attention in one case wherein operation was performed with the patient under local anesthesia. This soldier was semiconscious throughout the operation, which necessitated the removal from the left lateral ventricle of a small fragment of bone consequent to a shell fragment wound. Although 50,000 units of penicillin in 5 cc. of isotonic saline solution were introduced into the exposed ventricle and



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Operation was performed with the patient under one of three types of anesthesia: local (infiltration with procaine hydrochloride and block anesthesia), combined local and intravenous anesthesia (pentothal sodium), or ether-oxygen anesthesia (intratracheal, closed type).

Penicillin was placed intracranially in all wounds according to the following plan. If the brain was lacerated so that a ventricle was found to have been exposed or the foreign body entering the brain had traversed the ventricle, then 25,000 to 50,000 units of penicillin sodium dissolved in 5 c.c. of isotonic saline solution were introduced into the affected ventricle at the time it was surgically explored. If, however, a small missile had perforated a ventricle and lodged elsewhere and the damage in the cerebral tissue consequent to this was so small that open (visual) exploration of the ventricle was not considered advisable because of the increased trauma incurred by such operative intervention, then penicillin was injected into the ventricle through a ventricular cannula or a small catheter introduced along the track of the missile. Other deep cerebral wounds received 50,000 units of penicillin dissolved in 5 c.c. of isotonic saline solution directed into the wound, while more superficial wounds received a similar amount placed underneath the dura after its closure had been accomplished †.

Penicillin was also used in the scalp wound to irrigate the wound (250 units per cubic centimeter) and also after débridement and closure of the scalp

\*Two units of plasma dissolved in 250 c.c. of isotonic saline solution.

†In all instances the dura mater was closed, either by primary suture or with fascial grafts (temporal or fascia lata). Fibrin film was not available.

(10,000 units). Powdered penicillin (crystals) was occasionally sprinkled on uncovered areas of epicranium when there was excessive loss of scalp tissue but was not used as such intracranially. As the calcium salt of penicillin was not available I have not had any experience with its intracranial use such as has been reported by Cairns and his associates.<sup>3</sup>

I was not favorably impressed by the results of my earlier intracranial use of sulfonamides; hence, local sulfonamide therapy was not used in this series of craniocephal injuries.

The postoperative treatment included either oral or intravenous administration of sulfadiazine, in sufficient doses to maintain a concentration of 10 to 15 mg per 100 c.c. of blood and parenteral administration of penicillin. The latter was given intramuscularly in doses of 25,000 units every three hours as routine therapy. This treatment was continued for five to seven days. A few patients received from one to four intracisternal (cisterna magna) injections of 25,000 to 50,000 units of penicillin sodium in 5 c.c. of isotonic saline solution each, no patient received more than one injection a day.

#### CLINICAL OBSERVATIONS

It was not possible to follow these patients for a period sufficient to warrant the drawing of any definite conclusions about the incidence of infection and therapeutic efficacy of penicillin, for they were observed only from five to seventeen days in the evacuation hospitals. However, follow-up reports were received from many of them as late as three months after injury and personal follow-up was continued on a few to general hospitals; they were thus observed for thirty to sixty days. So far as I was able to determine there were no post-operative intracranial infections in any of these sixty-two cases. One patient, however, a Filipino boy, whose wound was eighteen hours old at the time he received definitive treatment, did have an infection of the scalp after two weeks. This was traceable to improper handling of the wound after he was transferred to a civilian hospital.

The anesthetists and I observed all of these patients closely at the time when penicillin was introduced into the brain. Particular attention was given to those who received penicillin by the intraventricular route. These observations failed to reveal any untoward effects following the local injection of penicillin into the brain, ventricles, and intracranial subarachnoid spaces at the time of the operation or subsequent thereto. Particular attention was paid to the pulse, respirations, blood pressure, occurrence of vomiting, and condition of the skin. If the patient was conscious, his state of consciousness was closely observed. At no time could we detect any evidence of a toxic or irritative reaction which could be attributed to the penicillin.

The innocuous nature of penicillin was forcefully brought to attention in one case wherein operation was performed with the patient under local anesthesia. This soldier was semiconscious throughout the operation, which necessitated the removal from the left lateral ventricle of a small fragment of bone consequent to a shell fragment wound. Although 50,000 units of penicillin in 5 c.c. of isotonic saline solution were introduced into the exposed ventricle and

later 25,000 units of penicillin were placed beneath the dura mater after it had been successfully closed there were no untoward effects. The pulse, blood pressure, respirations, state of consciousness, and condition of the skin remained unchanged. The postoperative course was uneventful, the temperature did not rise above 100.4° F., and his state of consciousness steadily improved. The maximal pleocytosis was 210 cells per cubic millimeter of cerebrospinal fluid (by lumbar puncture). In this case there was no penicillin introduced postoperatively into the cisterna magna or lumbar subarachnoid space. The scalp wound healed quickly by primary intention.

No toxic or irritative reactions were discerned in the other cases in which penicillin was administered by intraventricular method at the time of operation nor was there evidence of intracranial infection during the brief period in which the patients were observed. One patient, a young Filipino boy whose condition was poor at the time of operation, was observed to show an increase of pulse rate of about 15 per minute after 30,000 units of penicillin (in 5 c.c. of solution) had been placed into the left lateral and third ventricles; his general condition was not otherwise altered. He had an uneventful postoperative course save for a delayed infection of a scalp wound.

Penicillin was used locally in seven cases of compound (open) injuries of the frontal lobe which were complicated by extensive fractures of one or both cribriform plates and by similar involvement of the frontal or other accessory nasal sinuses. All of these patients were operated upon within fourteen hours of their injury. The wounds were explored through unilateral or bilateral transfrontal craniotomy with débridement of the brain and closure of the dura mater. In certain instances the closure of the dura mater necessitated the use of fascial transplants. Penicillin (50,000 units) was placed into the cerebral wounds and additional penicillin (23,000 units) was injected extradurally after closure of the scalp. There were no untoward symptoms in any one of the seven patients thus treated. All were observed for at least thirty days and at that time there was no evidence of infection or of leakage of cerebrospinal fluid in any of them. The wounds healed by primary intention.

Among the group who received penicillin by intracisternal methods (25,000 to 50,000 units) in the postoperative period only three complained of headache, nausea, and vomiting. In all of these cases there were a slight decrease of the pulse rate and an elevation of the respiratory rate. All symptoms were transitory except for headache, which persisted from one to four hours. The cell count of the cerebrospinal fluid did not disclose evidence of meningeal irritation from the penicillin for there was a steady decrease of the cell count, although none of the patients had had more than 1,000 cells per cubic millimeter at any time.

#### GENERAL CONSIDERATIONS

Minor toxic or irritative symptoms consequent to intracisternal, intraventricular, and intrathecal routes of administering penicillin have been recorded by Rammelkamp and Keefer<sup>1</sup> in 1943, Cairns and his associates in 1944,<sup>2</sup> and others.<sup>3,4</sup> In 1942, Florey and Jennings<sup>5</sup> showed experimentally that toxicity

decreases with increasing purity of penicillin. Cairns and his associates stated that "with intrathecal injections few reactions have so far been encountered and these also show variations depending presumably on particular impurities present in different batches." These workers also expressed the opinion that there may be serious damage in injecting large doses of penicillin into the ventricles because of reactions. More recently Johnson and Walker<sup>7</sup> have reported untoward effects following the introduction of 50,000 units of penicillin into the ventricles of a patient suffering from postoperative meningitis. This reaction was characterized by loss of consciousness and clonic seizures of the extremities with subsequent recovery. However, as has already been pointed out, Vogel and I<sup>8</sup> injected 100,000 units of penicillin into the cisterna magna in a single dose with only moderate and transitory reaction characterized by increased respirations, decreased pulse rate, mild fever, and headache. These symptoms were not alarming and could be avoided or minimized by decreasing the dose to 50,000 units or less. Furthermore, in this and other patients observed by us there was no evidence that penicillin increased the pleocytosis in the cerebrospinal fluid, for the cell count decreased coincidentally with the clinical improvement. Since the patient had shown a reaction to the intravenous injection of penicillin it was suggested that the reaction may have been due to impurities in the penicillin.\* It is also possible that these symptoms were due to a mild idiosyncrasy to penicillin. The observations made in the series of cases reported here lend credence to the suggestion of the presence of impurities in the penicillin.

Cairns and his associates observed a slightly different group of symptoms after ventricular injection of either sodium or calcium penicillin (250 or 500 units per cubic centimeter). "It consisted of patchy erythema of the skin of the trunk and limbs, often coming and going, generalized sweating, intermittent goose skin, slight rise of pulse rate and sometimes vomiting, the whole passing off in ten to twenty minutes." These observers attributed these symptoms to impurities in the solution and not to the penicillin, a conclusion which seems to be correct in the light of further observations. However, in two cases of meningitis not included in the series reported here, vomiting occurred following the intracisterna administration of 50,000 units of penicillin. This reaction was followed by moderately severe headache, which lasted about three to four hours. Decreasing the dose to 10,000 units did not alter the reaction in either case. These two are the only reactions of this type which I have encountered.

The observations herein recorded are entirely in accord with those recorded earlier by Florey and Florey,<sup>9</sup> Fleming,<sup>9</sup> Florey and Cairns,<sup>10, 11</sup> Keefer and his associates,<sup>12</sup> Evans,<sup>13</sup> Lyons,<sup>14</sup> Herrell, Heilman, and Williams,<sup>15</sup> and others<sup>3, 7, 16-18</sup>. However, none of these investigators have used as large amounts of penicillin in single doses as I have described here and elsewhere.† Pilcher

\*The penicillin received was frequently yellow orange or bright orange. A few patients who were given intramuscular and intravenous injections of penicillin made from these ampules of penicillin had febrile reactions with cutaneous reactions like those reported by Cairns and his associates.

†Since this was written the intracisternal injection of similar large doses of penicillin has been reported by Neymann, Heilbrunn, and Youmans<sup>19</sup> by Weackhardt,<sup>20</sup> and by others, with conflicting evidences of irritability and toxicity.

and Meacham<sup>3</sup> presumed from their experiments on dogs that the "transitory meningeal reactions are roughly proportional to the dose" of penicillin. Although this has not proved to be entirely correct it can be shown that in most of the cases in which there is a reaction to such large doses the symptoms may be diminished or avoided by a reduction of subsequent doses.

Several investigators<sup>2, 4, 5</sup> have shown that pleocytosis consequent to the inflammation of the meninges (in meningitis) decreases coincidentally to the recovery from the infection, thus strongly suggesting the lack of irritative effect of the penicillin. It is of interest, however, that the introduction of 10,000 units of penicillin into the subarachnoid space of normal persons produces remarkable pleocytosis.<sup>6</sup> Why the inflamed leptomeninges tolerate penicillin better than the normal meninges has so far not been explained. In view of these findings it was somewhat surprising to note the lack of a clinically demonstrable toxic or irritative reaction to penicillin introduced into the ventricles in cases of acute craniocerebral injuries. Here again one is led to suspect the presence of impurities in the penicillin used by those reporting these reactions. It would be of interest to repeat these studies now that a more highly purified product is available.\*

The necessity of using such large doses of penicillin as have been described here and elsewhere may justifiably be open to question and criticism. Rammelkamp and Keefer,<sup>4</sup> Keefer and his associates,<sup>5</sup> and others,<sup>6, 7</sup> have advocated the use of smaller doses, that is, 10,000 units or less<sup>10, 11</sup> given intrathecally once or twice a day. According to reports this dose seems to be adequate in the majority of cases.

However, it also has been shown that there is a hazard of penicillin fastness<sup>12, 13</sup> in certain bacteria and that this must detract the intrusiveness and effectiveness of the initial dose for all infections, particularly for staphylococci, streptococci, and pneumococci. Without laboratory control of the potency of penicillin as well as the bacterial susceptibility one cannot be certain what is the optimal or adequate dose in any given case. Certainly this is the situation with which the neurosurgeon is confronted when working, as he must, under field conditions, treating severely contaminated craniocerebral injuries and meningitis. One must consider all these craniocerebral wounds as grossly contaminated and in those cases in which patients receive the first definitive care after twenty-four hours one must consider the wounds as undoubtedly infected. It furthermore has been pointed out that the "proteolytic clostridia recovered

\*Since this paper was submitted for publication a considerable amount of literature has accumulated on the subarachnoid and intraventricular use of penicillin. From the work of Walker and his associates<sup>14</sup> it would appear that there is grave danger in the intraventricular, intracisternal and intrathecal injection of penicillin, particularly in using larger amounts of the antibiotic agent. Their work has been corroborated by others (Miller<sup>15</sup>, Reynolds and Moore<sup>16</sup>). However, some investigators have not encountered these severe reactions (convulsions, coma, death or even less severe reactions of fever, muscular twitchings, paralysis, pleocytosis in the cerebrospinal fluid, and so forth). From a review of these more recent contributions it would seem preferable to start penicillin therapy with smaller doses and gradually increase the concentration. It also has become evident that there are patients who are sensitive to pure crystalline penicillin. Thus the matter of impurities in penicillin as a cause for reactions seems to have been fairly well ruled out. Such reactions however appear to occur very infrequently and from my experience and those of others in using penicillin in deep in craniocerebral wounds (including the ventricles) I am not convinced that the risk of adverse reactions is great enough to outweigh the dangers of severe intracranial infections. Although the evidence presented here does not prove that patients with penetrating craniocerebral wounds are less likely to react unfavorably to penicillin, it may be that this is true.

from war wounds require four to five times as much penicillin as do *Staphylococci*.<sup>14</sup> Therefore, in view of the probability of the presence of proteolytic clostridia and of resistant strains of bacteria in craniocerebral injuries, as well as in traumatic meningitis and cerebral abscess, I believe that it is entirely justifiable to use the larger doses of penicillin. This is all the more true now that it has been shown that the untoward effects either are absent or, if present, are minimal and transitory.

#### SUMMARY

Clinical observations are detailed on the local application of large doses of penicillin in acute craniocerebral war wounds. In a series of more than 200 cases of cranial injury studied in the Southwest Pacific Theater of Operations, sixty-two patients had severe open (compound) craniocerebral injuries and all of these received penicillin into the intracranial wounds. Included in this group were nineteen cases in which one or more cerebral ventricles had been exposed or perforated by metallic fragments, bullets, or edged weapons (bayonets). Penicillin was placed into the ventricles of each of these patients in doses of 25,000 to 50,000 units. In no instance were untoward toxic or irritative reactions observed. In one case 100,000 units of penicillin were placed in the cisterna magna in the treatment of pneumococcal meningitis. Only transitory and mild untoward symptoms resulted and the patient recovered.

In view of the known contamination of war wounds with proteolytic clostridia and of the presence of resistant strains of bacteria which require many times as much penicillin as do other strains (susceptible strains), it is considered justifiable to use large doses of penicillin such as has been described in this report.

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## WAR WOUNDS OF THE CHEST

J. D. MARTIN, JR., M.D., ATLANTA, GA.

(From the Department of Surgery, Emory University)

THE early evacuation of casualties makes it difficult for the surgeon in an active theater of war to follow his cases for an adequate length of time. At a general hospital, however, it was possible to observe for a period of approximately three months or until their return to duty, or final disposition, 106 patients with war wounds of the chest. These were German prisoners of war who had been treated initially in hospitals near the front according to the established procedures of today. The common complications, the method of handling these complications, and the results are presented here.

It is necessary, first, to distinguish between simple penetrating wounds of the chest such as those produced by rifle bullets or other sharp missiles and massive wounds such as those caused by shell fragments. The simple penetrating wound, the type commonly seen in civil life, causes a minimal disturbance of the cardiorespiratory system. Treated by the so-called closed method, a large number of these patients will recover without subsequent surgery. In military practice, however, the second type is more common and many will require later operative procedures since convalescence is associated with a variety of complications. In the massive wounds of the chest, disturbance of physiology is of paramount importance and it is essential to repair the damaged viscera and close securely the thoracic cavity in order that the cardiorespiratory system may function adequately. It should be noted, however, that, depending on its course, a small missile may seriously damage a vital organ. Frequently with shrapnel wounds there is an associated blast injury which produces further disturbance in the cardiorespiratory mechanism and the late complications of recurrent hemothorax. Hemothorax may result in dense fibrous pleuritis around the lung, with a collapse of the lung which must be corrected.

Chest wounds are of greater importance because serious complications are more commonly encountered here than in any other part of the body. The initial treatment is of great importance but the follow-up and continued observation require much consideration as sequelae should not be minimized. The associated trauma to other parts of the body further complicates the treatment of chest wounds but the initial therapy should be directed toward the thorax before treatment of other injuries is undertaken.

The shock encountered in chest wounds is usually out of proportion to that of wounds elsewhere. For purposes of classification, the shock in these cases may be divided into that due to hemorrhage and that due to disturbance in the cardiorespiratory mechanism. The usual evidences of shock, such as lowering of the blood pressure and decreased cardiac output, and the concentration of the red cells, are not at first demonstrated in individuals with penetrating wounds of the chest. This may be because, with the suddenness and



TABLE III. SECONDARY OPERATIONS

Decortications	16
Drainage of empyema	14
Drainage of subphrenic abscess	5
Drainage of lung abscess	2
Removal foreign body of lung	2
Repair of diaphragmatic hernia	1
Total	40

Resuscitation is accomplished by the administration of whole blood in quantities sufficient to restore the loss and to correct the existing shock. The first 500 c.c. can be administered at the normal rate but all subsequent transfusions must be given slowly in order not to overload the already damaged respiratory mechanism. Early aspiration of the tracheobronchial tree, either with a catheter or by means of bronchoscope, will aid considerably in diminishing the difficulty of breathing. Oxygen, of course, may be beneficial at this time to decrease the hypoxia while preparing the patient for a definite operative procedure.

Closure of the sucking wounds may be accomplished satisfactorily by the application of tight pressure dressings which can be held in place until a more definitive closure is accomplished. Many a penetrating wound becomes a sucking wound as soon as débridement is undertaken. With small wounds of entrance there frequently may be a large wound through the intercostal spaces that perhaps may be sealed by the muscles on the posterior and lateroposterior chest wall. Débridement must be done carefully removing all skin, damaged muscle, and loose rib fragments. Closure of the pleura is not easy, but the use of the intercostal muscles and pleura and the accessory muscles of the chest wall when closed in layers will satisfactorily effect a closure of the thoracic cavity. It is most essential to close all of the layers on the anterior chest wall because so frequently a disruption of the chest wall will occur due to its normal respiration motion. Wounds have been seen to disrupt and develop an open pneumothorax in one week to ten days after the original closure of the anterior pleura and the intercostal muscle, when the accessory muscles and skin were not effectively closed.

Intercostal nerve blocks relieve the patient of the immediate pain and allow for a more complete respiratory effort, early coughing, and the removal of retained blood and secretions from the bronchi. In the open thoracotomies, the procedure can be accomplished easily by the injection of 1 per cent procaine in the intercostal spaces from within. In those in whom an open thoracotomy was not performed, an injection of two to three intercostal spaces above and below the levels of the wounds of entrance and exit is advisable. This procedure can be repeated daily depending on the symptoms.

In order to prevent late complications it is essential to aspirate as nearly as possible all retained blood and air. At the time of the initial treatment the chest should be rendered as free of blood and air as is possible. In so many instances the blood becomes organized and compresses the lung, resulting in atelectasis. In the collapsed lung serious impairment of function occurs and there is a likelihood of prolonged disability. The presence of blood predisposes

to infection and frequently massive empyema develops. The intramuscular administration of penicillin in 25,000 unit doses every three hours is routine. At the time of aspiration 40,000 units may be injected into the pleural cavity and repeated with each subsequent aspiration. However, penicillin cannot be satisfactorily employed intrapleurally when drainage tubes are in use; to clamp the tube will result in the development of a blood clot obliterating the lumen, thus destroying its usefulness as a drain.

It is most important that the use of drains be made with due consideration of their purpose and a knowledge of their benefit and at the same time with regard to their dangers. When a forward thoracotomy is done a larger tube should be brought out at the dependent portion and attached to an underwater seal. The purpose of this tube is to allow removal of the accumulated blood and at the same time to maintain continued expansion of the lung. This tube will function as a drain from twenty-four to forty-eight hours, after which time either the lung becomes fixed or the tube becomes plugged with clotted blood. This state is noted by a cessation of the oscillations of the water column. The tube should be removed at this time because if allowed to remain in for a longer period, the likelihood of infection will be increased. The insertion of a small anterior drain in the second intercostal space will further decompress the accumulated air and prevent the formation of a tension pneumothorax if damage to the underlying lung exists. This tube also should be removed at the earliest moment to prevent infection.

An analysis of the initial treatment of those patients is interesting in that in 68 the initial treatment was that of simple débridement and a closure of the sucking wounds when they existed. An open thoracotomy was performed in 38 cases for various reasons; it was necessary to repair the diaphragm in 9 instances, to suture the lung in 7 instances, and to remove the spleen in 6 instances. Drainage of the liver was done by the subdiaphragmatic route in 6 cases. Foreign body was removed from the lung in only 2 cases. The stomach was sutured through the transdiaphragmatic opening in 1 instance. This analysis does not separate those cases that were directly associated with the wound in the chest. There has been much discussion in regard to the advisability of a formal exploration of the thoracic cavity as the primary treatment. This procedure carries with it a certain danger and perhaps allows for more frequent complications than are probable in patients in whom thoracotomy was not done. Aside from the fact that these patients usually are not in good condition to withstand long operative procedure, it is believed that most corrective surgery could best be withheld until the patient's chances for making complete recovery are greatest. The usual indications for forward thoracotomy are the presence of an increasing uncontrollable intrathoracic hemorrhage, the complete débridement of the pleura where rib fragments and foreign material are present and the transdiaphragmatic wounds in order to explore this region for possible damage to viscera both above and below the diaphragm. The presence of a small metallic foreign body as such is not necessarily a reason for early thoracotomy. In suspected damage of the pericardium or the mediastinal structures, immediate explorations are governed by the symptoms presented, namely, those of cardiac

TABLE I. WOUNDS OF CHEST

Total cases	106
Mortality	.0%
Total infection	22.6%
Empyema	20.7%
Returned to duty within 120 days or less	72.5%

severity of the shock, insufficient time is allowed to manifest all of the changes after the injury. In other words, following the massive trauma, the shock is critical or the damage done is not irreparable. The hemorrhage encountered is of variable degree and type. In civil cases the hemorrhage present is more often of the controllable type, that is, a moderate nonprogressive, internal blood loss, which ceases without operative procedure, unless vital organs are involved. Bleeding directly from the parenchyma of the lung usually ceases spontaneously. In the uncontrollable type, such as bleeding from an internal mammary or intercostal artery or from a larger vessel in the thorax, the shock is progressive and fails to respond to the usual method of restoration. It is particularly important in these cases to operate as early as possible in spite of the presence of shock. However, attempts at replacing blood and maintaining circulatory volume should always be made. Intrathoracic hemorrhage may mechanically interfere with the function of the heart and the aeration of the other lung.

Intrapericardial bleeding produces marked symptoms from a small blood loss. If, from a small penetration of the pericardium, the blood collects within the sac, cardiac tamponade results, this is manifested by distant cardiac sounds, apparent increase in the size of the heart, lowering of the cardiac output, and distention of the veins of the neck, evidence of an increase in venous pressure. This condition is an urgent emergency and must be corrected immediately if the patient is to survive the pressure of the blood within the pericardium. On the other hand, if the wound in the pericardium is very large and there is no wound of the heart muscle, evidences of the tamponade cannot be demonstrated. The blood, instead of distending the pericardial sac, accumulates in the pleura.

There are many manifestations of disturbed cardiorespiratory mechanism. The production of an open pneumothorax is the most common of all these disturbances, positive pressure is produced within the thoracic cavity by the entrance of atmospheric air. Air is brought into the chest on inspiration and expelled with expiration, that is, a so-called sucking wound results. This positive pressure is exerted on the large vessels and decreases the amount of blood entering the heart. The lungs may become partially deflated and inadequate oxygen exchange occurs. The immediate closure of these openings is essential if the effects are to be minimized. The amount of shock varies directly with the size of the opening in the thorax.

The development of a tension pneumothorax may be manifested immediately after the trauma or it may be exhibited several hours or days after the injury. These conditions are produced by a flap tear in the lung which acts as a trap and allows the entrance of air from the lung into the pleural cavity without the opportunity of escape. The increasing pressure within the thorax must be

recognized and relieved at the earliest possible moment. Any abnormal variation of thoracic pressure on the two sides may be a contributing factor. Combined abdominal and thoracic wounds may cause further disturbance of the function of the chest by creating a positive pressure on one or both sides. Injuries to the diaphragm as such or injuries to the innervation of the diaphragm may produce a paralysis of the muscle which results in the paradoxical motions. Acute manifestations of this add to the increasing shock associated with these wounds. Cardiac tamponade, as already noted, may contribute to the disturbance of cardiorespiratory mechanism.

It is essential to determine the degree of shock and the ability to relieve it before undertaking any surgical procedure. In those in whom hemorrhage is uncontrollable, operation may be undertaken immediately, however, a certain number may be safely handled after the patient has completely responded to the immediate treatment. In many instances it is impossible to estimate the extensiveness of a lesion until operation. However, determination can be made and the proper procedure outlined as soon as satisfactory examinations, including x-ray, have been completed.

A group of 106 patients, treated in a general hospital, are being reported in detail. The mortality was 0.9 per cent. Since all these patients were German prisoners of war, many had had a delay in the initial forward treatment, varying from twelve to forty-eight hours, due to the exigencies of battle. It is noted that the percentage of infection was high, 22.6 per cent. Empyema accounted for 20.7 per cent, and infection of the lung or of the chest wall for the remainder. This percentage is unusually high, it may be partially explained by the delay in the initial treatment. However, chemotherapy, instituted in all cases, minimized the severity of these infections and permitted earlier surgical procedures, thus producing more complete recovery. The results obtained were reflected in the percentage of patients (72.5 per cent) returned to duty in 120 days or less. Of the remaining 27.5 per cent the chest wound was not the only factor preventing their return to duty. Injury to the spinal cord or brachial plexus, fractured femurs, and, in one instance, acute psychosis were some of the associated problems. The initial treatment in each of these cases was the same as if performed routinely in the care of the American battle casualty.

The treatment in the forward hospitals may be divided into the following categories: first, resuscitation, second, closure of sucking wounds; and third, the débridement of the damaged structures to the chest wall and the underlying viscera.

TABLE II ORIGINAL OPERATIVE PROCEDURES

Débridement and closure of sucking wounds	64
Thoracotomy	38
Repair of diaphragm	9
Suture of lung	7
Splenectomy	6
Drainage of liver	0
Removal foreign body of lung	2
Nephrectomy	1
Suture of stomach	1

TABLE III. SECONDARY OPERATIONS

Decortications	16
Drainage of empyema	14
Drainage of subphrenic abscess	5
Drainage of lung abscess	2
Removal foreign body of lung	2
Repair of diaphragmatic hernia	1
Total	40

Resuscitation is accomplished by the administration of whole blood in quantities sufficient to restore the loss and to correct the existing shock. The first 500 c.c. can be administered at the normal rate but all subsequent transfusions must be given slowly in order not to overload the already damaged respiratory mechanism. Early aspiration of the tracheobronchial tree, either with a catheter or by means of bronchoscope, will aid considerably in diminishing the difficulty of breathing. Oxygen, of course, may be beneficial at this time to decrease the hypoxia while preparing the patient for a definite operative procedure.

Closure of the sucking wounds may be accomplished satisfactorily by the application of tight pressure dressings which can be held in place until a more definitive closure is accomplished. Many a penetrating wound becomes a sucking wound as soon as débridement is undertaken. With small wounds of entrance there frequently may be a large wound through the intercostal spaces that perhaps may be sealed by the muscles on the posterior and lateroposterior chest wall. Débridement must be done carefully removing all skin, damaged muscle, and loose rib fragments. Closure of the pleura is not easy, but the use of the intercostal muscles and pleura and the accessory muscles of the chest wall when closed in layers will satisfactorily effect a closure of the thoracic cavity. It is most essential to close all of the layers on the anterior chest wall because so frequently a disruption of the chest wall will occur due to its normal respiration motion. Wounds have been seen to disrupt and develop an open pneumothorax in one week to ten days after the original closure of the anterior pleura and the intercostal muscle, when the accessory muscles and skin were not effectively closed.

Intercostal nerve blocks relieve the patient of the immediate pain and allow for a more complete respiratory effort, early coughing, and the removal of retained blood and secretions from the bronchi. In the open thoracotomies, the procedure can be accomplished easily by the injection of 1 per cent procaine in the intercostal spaces from within. In those in whom an open thoracotomy was not performed, an injection of two to three intercostal spaces above and below the levels of the wounds of entrance and exit is advisable. This procedure can be repeated daily depending on the symptoms.

In order to prevent late complications it is essential to aspirate as nearly as possible all retained blood and air. At the time of the initial treatment the chest should be rendered as free of blood and air as is possible. In so many instances the blood becomes organized and compresses the lung, resulting in atelectasis. In the collapsed lung serious impairment of function occurs and there is a likelihood of prolonged disability. The presence of blood predisposes

to infection and frequently massive empyema develops. The intramuscular administration of penicillin in 25,000 unit doses every three hours is routine. At the time of aspiration 40,000 units may be injected into the pleural cavity and repeated with each subsequent aspiration. However, penicillin cannot be satisfactorily employed intrapleurally when drainage tubes are in use; to clamp the tube will result in the development of a blood clot obliterating the lumen, thus destroying its usefulness as a drain.

It is most important that the use of drains be made with due consideration of their purpose and a knowledge of their benefit and at the same time with regard to their dangers. When a forward thoracotomy is done a larger tube should be brought out at the dependent portion and attached to an underwater seal. The purpose of this tube is to allow removal of the accumulated blood and at the same time to maintain continued expansion of the lung. This tube will function as a drain from twenty-four to forty-eight hours, after which time either the lung becomes fixed or the tube becomes plugged with clotted blood. This state is noted by a cessation of the oscillations of the water column. The tube should be removed at this time because if allowed to remain in for a longer period, the likelihood of infection will be increased. The insertion of a small anterior drain in the second intercostal space will further decompress the accumulated air and prevent the formation of a tension pneumothorax if damage to the underlying lung exists. This tube also should be removed at the earliest moment to prevent infection.

An analysis of the initial treatment of those patients is interesting in that in 68 the initial treatment was that of simple débridement and a closure of the sucking wounds when they existed. An open thoracotomy was performed in 38 cases for various reasons; it was necessary to repair the diaphragm in 9 instances, to suture the lung in 7 instances, and to remove the spleen in 6 instances. Drainage of the liver was done by the subdiaphragmatic route in 6 cases. Foreign body was removed from the lung in only 2 cases. The stomach was sutured through the transdiaphragmatic opening in 1 instance. This analysis does not separate those cases that were directly associated with the wound in the chest. There has been much discussion in regard to the advisability of a formal exploration of the thoracic cavity as the primary treatment. This procedure carries with it a certain danger and perhaps allows for more frequent complications than are probable in patients in whom thoracotomy was not done. Aside from the fact that these patients usually are not in good condition to withstand long operative procedure, it is believed that most corrective surgery could best be withheld until the patient's chances for making complete recovery are greatest. The usual indications for forward thoracotomy are the presence of an increasing uncontrollable intrathoracic hemorrhage, the complete débridement of the pleura where rib fragments and foreign material are present and the transdiaphragmatic wounds in order to explore this region for possible damage to viscera both above and below the diaphragm. The presence of a small metallic foreign body as such is not necessarily a reason for early thoracotomy. In suspected damage of the pericardium or the mediastinal structures, immediate explorations are governed by the symptoms presented, namely, those of cardiac

TABLE IV. COMPLICATIONS

<i>33 Early Thoracotomies</i>	
Empyema	9
Constricting pleuritis	7
Bronchial fistula	5
Lung abscess	2
Subphrenic abscess	2
Tension pneumothorax	1
<i>68 Conservatively Treated Patients</i>	
Empyema	13
Constricting pleuritis	7
Bronchial fistula	6
Subphrenic abscess	3
Lung abscess	1

TABLE V. AVERAGE PERIOD OF HOSPITALIZATION

Hemopneumothoraces	82 days
Decorticated cases	52 days
Empyemas (decorticated)	58 days
Empyemas (open drainage)	100 days

tamponade or other associated disturbances of the cardiorespiratory mechanism. An analysis of the complications of the forward thoracotomies compared with those not receiving a forward thoracotomy were similar.

There were thirty-eight cases of early operation, empyema developed in nine, bronchial fistula in five, subphrenic abscess in two, a chronic fibrous pleurisy with associated atelectasis in seven, and tension pneumothorax in one case.

The complications of the 68 conservatively treated patients were as follows: Empyema developed in 13, lung abscess in 1, bronchial fistula in 6, subphrenic abscess in 3, chronic fibrous pleurisy with atelectasis in 7. This comparison indicates that there is not a great deal of difference in the number of complications.

It is interesting to note that of the 106 patients, 78 had repeated aspirations. The average number of aspirations per case was 3+. The average blood removed in any one case was 6,350 c.c. (this patient developed a total empyema necessitating decortication). The greatest number of aspirations in one case was 20, empyema developing on both sides was corrected by rib resection with recovery. It is noted that if the first aspiration yields a greater amount of blood and subsequent aspirations decrease in amount, the prognosis is generally good. However, this does not always hold true because organization of the clot may prevent aspiration. Continued refilling in spite of aspiration is significant in that organization is continuously taking place and the likelihood of expanding the lung compressed for a long time is not good. If the fluid increases in amount, it will probably be necessary to perform decortication.

In spite of excellent care in the forward hospitals, there are many necessary procedures which are essential for the purpose of shortening the convalescence and also of preparing those patients in whom late operations are indicated. The most essential problem is that of improving the patient's general condition as

much as possible before undertaking any operative procedure. In most instances where the hematocrit and total red count indicate a rather marked anemia, the blood should be returned to its normal levels by repeated transfusions. It is still necessary to give blood with much precaution during this period, as in the beginning. Many patients require as much as 1,500 to 2,000 c.c. of blood before the hematocrit is raised to 45 volumes per cent. The administration of proteins and vitamins is of much importance. Aspirations should be continued in those patients who continue to show evidence of either fluid or air. Many of these patients can avoid secondary operations if this effort is continued at this stage. Within two to three weeks after injury one is able to estimate the most likely outcome. It is felt that the injection of air following aspirations should not be done because it further delays expansion.

Penicillin is administered routinely in all patients who show evidence of sepsis but it is felt that such therapy alone will not substitute for adequate removal of infected blood in the pleura or an infection within the lung. The persistence of hemopneumothorax alone is not an indication for either penicillin or the sulfanilamides. These should not be given routinely over a long period of time. Particularly is this true in individuals in whom a residual amount of blood remains in the pleura without evidence of sepsis. Before and after removal of foreign bodies, penicillin is administered as a prophylaxis and lessens the likelihood of reinfection of what dormant infection might have been present. If there is a low-grade infection following aspiration, penicillin may be instilled into the pleural cavity with beneficial results. When the lung has been fixed and further expansion seems impossible, the prolonged intrapleural injection of penicillin is not indicated. It is well to evaluate each case and to withhold penicillin unless there are definite indications.

Of the 106 cases, it was necessary in the fixed hospital to perform major operative procedures in 40. There were 16 cases of decortication, 14 of drainage of empyema, 5 of subphrenic abscess, 2 of lung abscess, and 2 of foreign bodies of the lung, 1 diaphragmatic hernia was repaired. It is necessary, therefore, that many of these patients be prepared as quickly as possible to increase their chances for early surgery and also to lessen the chances for secondary operations. Within a period of four to six weeks after the injury, the outcome can be fairly well determined. That is, the chest has been aspirated dry and a residual hemothorax or diaphragmatic hernia can be detected, the necessity for removal of remaining foreign bodies can be determined, or the likelihood of septic process developing from hematomas or foreign bodies within the pleura or lung estimated. Taking into account the original thoracotomies performed in a forward hospital and those performed in the general hospital, a total of 27 major procedures were performed in the 106 cases. This number apparently is somewhat large but it is felt that, because of the type of wounds encountered and also the time lag before the initial treatment, this number is in keeping with the general experience of others.

The results obtained in chest wounds are perhaps over-all as good as those obtained in any group of war injuries. If the patient survives the immediate effect of trauma and has had adequate treatment, both in the forward and rear





ture of ceepryn did not sterilize the skin more effectively than did the usual method of painting the skin with the antiseptic

This failure to increase the efficiency of the skin sterilization by scrubbing with the antiseptic is at variance with the results obtained by Helmsworth and Hoxworth.<sup>9</sup> These authors obtained positive cultures from 58.2 per cent of the cases when the skin was painted with 1-1000 tincture of ceepryn and from 37.7 per cent when it was painted with 1-500 tincture of ceepryn. But when the skin was scrubbed for five minutes with a 1-100 aqueous solution, positive cultures were obtained from 10.3 per cent of the skin fragments and after a ten-minute scrub with the 1 per cent aqueous solution the percentage of positive cultures was reduced to 5.4 per cent. It is thus evident that prolonged scrubbing of the skin with a 1-100 aqueous solution of ceepryn is more effective than painting or a short two-minute scrubbing with the tincture of ceepryn 1-1000.

Staphylococci were the predominant organisms in these cases and appeared in 68, or 17 per cent, of 398 cultures, 63 of these were *Staphylococcus albus* and 5 were *Staphylococcus aureus*. In two instances diphtheroids also grew in the cultures which contained *Staphylococcus albus*. In the remaining twenty-four positive cultures, the organisms identified were hay bacilli, nine; *Bacillus subtilis*, five; diphtheroids, five; *Streptococcus viridans*, one; *M. sarcinae*, one; *Micrococcus tetragenus*, one; *M. catarrhalis*, one, and moulds, one. Some of these especially the hay bacilli, were undoubtedly contaminants.

From observation as reported in this paper and from experience in using it, tincture of ceepryn 1-1000 is an efficient and satisfactory antiseptic for the preoperative preparation of the skin. No ill effects have been noted from its use for this purpose in several hundred patients and its stain can be removed with relative ease with soap and water. It does not, however, completely sterilize the skin, nor does any other skin antiseptic with which we are familiar. The bacteria, mostly *Staphylococcus albus*, which are embedded deep in the hair follicles are not killed by the antiseptic which is applied on the surface, and observations indicate that scrubbing of the skin for two minutes with the tincture of ceepryn 1-1000 does not increase the efficiency of the skin sterilization.

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# Recent Advances in Surgery

CONTRIBUTION TO THE SURGICAL TREATMENT OF

## HYPERPARATHYROIDISM

A REVIEW OF THE PROGRESS OF SURGICAL TREATMENT IN THE PRESENT STATE OF  
KNOWLEDGE OF THE DISEASE

FRANK MARSH, M.D., ASSISTANT CLINICAL PROFESSOR

(First of the Surgical Department, B. Z. Babcock Kansas University Hospital)

### HISTORICAL INTRODUCTION

THE study of the problem of hyperparathyroidism and its treatment by parathyroidectomy falls into three groups: (1) The discovery made in the study of metabolic affections of the skeleton; (2) The recognition of an anatomic relationship between the parathyroid glands and their tumors, on the one hand, and certain diseases of the skeletal system, on the other; and (3) the closer insight gained into the relationship existing between the parathyroids and the calcium metabolism.

A synthesis of results achieved in these three fields of research, although with different speed, led to the first successful parathyroidectomy in a case of Recklinghausen's disease in which a parathyroid tumor could be removed (Mandl, 1923). Since that appeared, the patient recovered completely, a number of problems involved seemed to be solved—a fact that was of greatest importance for practical surgery.

But, to return to the development outlined, only the third point is of particular interest for this study.

There can be no doubt that Reckling (1906) was the first to recognize the relationship between the parathyroid glands and the calcium metabolism, rather than other authors often mentioned in the literature. Since his studies were later, in a positive as well as negative respect, of greater importance to the development of parathyroid surgery they shall be dealt with in detail. It shall be seen later how great their importance is even today although Reckling's theory, as far as it concerned the treatment of hyperparathyroidism, could be discarded.

Enthelm's fundamental experiments on rats consisting in extirpation as well as homotransplantation of parathyroid tissue very definitely brought certain skeletal changes in the experimental animals. To begin with, after parathyroidectomy they consisted in defects of the enamel of the teeth, but later changes involving the entire skeleton. This was a fact from which Reckling drew his well known conclusions.

Reckling and Voegtlin later, in 1909, established a definite relationship between calcium metabolism, parathyroidectomy being followed invariably by a decrease in the calcium level of the blood. They were able further to demonstrate the excretion of the quantitative amount of calcium in the urine and this condition was reflected in the blood.

These findings were verified by a number of other authors who did not add, however, substantially to the knowledge on the subject.

It is generally known that Collip's great discovery (1925),\* the isolation of the parathormone, marked a turning point in the therapy of tetany. It further furnished the basis for many experiments which greatly improved the knowledge on the pathologic conditions in question. The experimental production in animals of a state to a certain extent coinciding with that of hyperparathyroidism was considerably facilitated by the use of Collip's parathormone in its various modifications (Jaffe, Bodansky and Blair, Johnson and Wilder, Mandl and Uebelhör and others).

Now there remains only the question of how parathyroid tumors or enlargement, when it was chanced upon during autopsy, was explained around 1925. No distinction was made by the majority of authors between the different malacias of the bone system and, following Erdheim's theory, the enlargement of the parathyroid glands was regarded as the consequence rather than the cause of the skeletal changes.

It was Erdheim who pointed out that the disturbance of the calcium metabolism preceded the enlargement of the parathyroids and increased gradually only to subside after rickets (the disorder with which Erdheim was preponderantly concerned) was cured. The parathyroids produce the secretion essential for the calcification of bones which in the malacias is used pathologically. Rickets, therefore, would be characterized by an intensified requirement of functioning parathyroid substance; the hyperplasia or hypertrophy of the glands would, therefore, constitute a compensatory reaction destined to cope with the additional strain placed upon the organs; parathyroid enlargement might, therefore, be paralleled to compensatory hypertrophy in general.

This theory of Erdheim which was approved by other authors was also applied to Recklinghausen's disease.

In treating patients suffering from this disease my first thought was to support the gland in its task of controlling the calcium metabolism by administering a potent parathyroid extract to the organism. My idea was that, should this procedure prove a failure, that fact would indicate (contrary to Erdheim's theory) that the new growth found in the parathyroid was to be considered the primary factor therefore, that nothing but removal of the parathyroid tumor would be effective in setting the disturbed calcium metabolism in order again and curing the disease.

#### CASE REPORT

A patient with disturbed calcium metabolism was admitted to department in October, 1924. Treatment with Collip's parathormone was tried, but with absolutely no result, none of the symptoms improving.

In July, 1925, four parathyroid glands, taken from another patient admitted to the hospital in a moribund condition, were implanted into the abdominal wall. None of the symptoms disappeared; the calcium content of the urine remained unchanged.

On July 30, 1925, a parathyroid tumor (measuring 25 by 15 by 12 mm) was removed from the left inferior area behind the thyroid gland. On macroscopic examination this was diagnosed as an adenoma.

\*Editorial comment: It is only fair to state that Dr. A. M. Hanson should be credited with the independent discovery of the parathyroid hormone.

As early as a few days after the operation, the patient's condition began to improve. The calcium content of the urine and the calcium level of the blood were considerably lower. The patient felt better. No symptoms of tetany appeared. As early as four months later, roentgenograms showed denser lime shadows of the bones than before operation. The severe pain of the bones previously present also subsided. For the first time in years the patient was able to sit up in bed and to walk about on crutches.

The patient was readmitted to the hospital\* in February, 1926, because of renal calculi and severe arthrosis of the knee joint. Continuous roentgen control, however, revealed improvement of the skeletal symptoms. The general condition was also good and the calcium metabolism normal. In view of a certain amount of doubt expressed by a number of authors in the literature concerning the significance of the operative procedure, the patient was watched very carefully and exact determinations were made of the calcium and phosphorus proportion in the blood and urine. The renal disturbance subsided after conservative treatment and the patient was discharged soon after.

At that time the patient's sister developed *ostitis fibrosa localisata* of the tibia which gave rise to spontaneous fracture of the bone. This *ostitis fibrosa localisata* (not Paget's disease) later resulted in the growth of a sarcoma which made it necessary to amputate the leg.

In the patient with *morbus Recklinghausen*, however, the lime content of the skeletal system continuously increased as time went on, so much so that it was thought that the case might not present *morbus Recklinghausen* at all but Paget's osseous disease†. This view was opposed vigorously‡ on the theory that it may have been that the skeletal system with its severe lime deficiency accumulated, after the successful operation, such excessive amounts of calcium that the picture became strongly indicative of pseudo Paget §.

After six years of improvement the patient's condition grew worse. By September, 1932, he once more had a renal calculus. There was hypercalcemia again, the phosphatase level of the blood was lowered, the bones once more became decalcified, and the patient was incapacitated.

With the thought that there would be another parathyroid tumor, the patient was operated upon again (Oct 18, 1933). Since, however, none was found, neither in the entire neck region nor in the mediastinum, a large portion of the thyroid gland was removed with the intention of thus removing simultaneously an intrathyroidal adenoma should there be one. Actually, microscopic examination made clear that two parathyroid glands had been removed by this thyroidectomy. The one had been situated within the thyroid tissue, the other just touched the outer area. The former was more than normal size but there were no other pathologic findings ||.

It was significant that (1) after operation no tetany developed although the patient had been deprived of three of the thyroid glands. It was, therefore, obvious that somewhere in the organism there must have been a substantial amount of active parathyroid tissue, (2) although the parathyroid activity had been greatly reduced there was no improvement in condition and no change of the pathologic calcium metabolism. (Today we are well acquainted with the fact that removal of normal parathyroid tissue is not likely to influence this condition—a fact that supports the theory that the parathyroid tumor is the primary factor in creating the disturbance.)

No improvement was attained and the patient succumbed in February, 1936. Autopsy¶ did not reveal parathyroid tissue or a parathyroid tumor anywhere in the body although all sites where the misplaced organ could be expected to be present were carefully inspected.

\*The author reported this case in the *Zentralblatt für Chirurgie* (1926). However, it is described further here since in this patient unfortunately the process ran an unusual course, apart from the immediate postoperative improvement, which persisted for six years.

†Opinion expressed by Kienbock.

‡Mandl Beitr z klin Chir, 1934.

§In this the author has been supported by Snapper, Chifoliau and Braine, and others.

||According to C. Sternberg's view.

¶The autopsy records with a number of photographs taken at every stage were unfortunately lost at the Institute in Vienna.

In later similar cases with the same immediate results and a rather similar clinical and chemical-pathologic aspect, the patients were operated upon and within a few years it was generally agreed upon that, as we call it now, "the osseous type of hyperparathyroidism" calls first of all for removal of a parathyroid adenoma. Publications on operations of this kind up to 1932 (see Lièvre, 1932) were made by Eiselsberg-Gold; Barr, Bulger and Dixon; Boyd, Milgram and Stearns, Eggers, Wilder; Snapper; Hunter; Barr and Bulger; Lièvre and Chifoliau; Compere; Pemberton and Geddie; Disque, Sainton, Bourguignon and Millot, Lièvre, Quiek, Hundsberger and Schnabel, Hunter and Walton; Snapper and Boere. Clinically, the aspect offered by all these cases is rather uniform. In the majority of them the onset is with pain in the bones and extremities and great lassitude. There are further attacks of vomiting and occasionally the history contains reference to symptoms of the urogenital system. Polydipsia and polyuria are just as often mentioned as renal calculi which, however, and this should be particularly stressed, in the majority of cases have occurred a long time before and play no decisive role at all at the time when the patient is examined and the diagnosis made.

Extraordinarily frequently spontaneous fracture is reported as the first sign of the disease which is often the only reason for consulting a physician. Roentgenograms often reveal skeletal changes of the Recklinghausen type (cysts, brown tumors, softening of the skeleton characterized by deformation of the long tubular bones).

Other criteria of hyperparathyroidism are hyperealecemia, hypophosphatemia, hyperealeiuria and hyperphosphaturia, increased phosphatase in the blood serum.

In case an encapsulated tumor is palpable in the neck region this is usually part of the thyroid gland since parathyroid tumors only rarely offer palpatory findings (see under technique of parathyroidectomy).

Where a parathyroid tumor could be removed operatively, it was particularly the negative calcium balance that was rapidly normalized. The calcium level of the blood soon dropped and the calcium elimination in the urine became less. Within six to twelve months the bones showed an increased calcium content and their structure gradually became normal. This fortunate development is not, however, encountered invariably.

#### DEVELOPMENTS AFTER 1932

Very probably, the synopsis of cases given previously includes only the successful ones. Very little is known about the proportion of failures and Churchill was presumably right when he said, "A brief period of confusion then followed during which surgical endeavours were controlled by neither pathological findings nor chemical data. In their eagerness to explore a new territory surgeons became incautious and floundered in a field beset with pitfalls and blind alleys."

Churchill and Cope, though, in 1934 reported eleven operations. In all of them an adenoma of one or two parathyroids was found which had to be considered the factor responsible for the derangement of the calcium and phos-

*phorus* metabolism, and *normalization* was invariably achieved after removal of the adenoma. Attention was also drawn by these authors to the abnormal localization of the parathyroid tumors to which I referred in 1933. Churchill and Cope (1934) emphasized the danger with which operation is fraught in the presence of an abnormal localization and advised surgeons to be careful not to remove normal parathyroid tissue should they be unable to detect a parathyroid adenoma.

The further development of parathyroid surgery as well as the study of hyperparathyroidism, as it were, lay in the hands of the staff of the Massachusetts General Hospital where by a teamwork of all departments new light was thrown on all problems involved.

Thus, in 1934, Albright, Bloomberg, Castleman, and Churchill were the first to draw attention to cases in which hyperparathyroidism was not, as it had up to then been the rule, associated with an adenoma of one or, although rarely, two parathyroids but that there existed a variety of hyperparathyroidism characterized by hypertrophy of the entire parathyroid tissue. Cases of two parathyroid adenomas had already been referred to by Hellström and also by Hunter but these novel findings had up to then been unknown. There was no adenoma but a general hyperplasia of the entire parathyroid tissue characterized histologically by "uniformity of the structure, the enormous size of the cells, and extreme clearness of the cytoplasm." On the strength of findings obtained in three cases these authors expressed the opinion that from that time on hyperplasia of the parathyroid glands with hyperparathyroidism should be regarded a disease entity. This seems justified particularly as clinically the three cases presented a number of similar features; the bone changes were completely overshadowed by the "renal type" of hyperparathyroidism.

Cope, of the same group of investigators, in 1935 reported upon twenty-seven operations for hyperparathyroidism. In this series the classical picture with one or maximally two adenomas occurred twenty-one times while the cases of "hyperparathyroidism associated with hyperplasia of the entire parathyroid tissue" had risen to six. Again, in the latter group, renal calculi governed the scene along with normal or nearly normal bone findings. The disturbance of the calcium-phosphorus metabolism is the same as in the classical type to become normalized after reduction of the parathyroid tissue.

In 1936 the number of cases reported by Churchill and Cope had risen to thirty. Ten of these cases were of the classical type, skeletal findings with or without renal complications predominating while eighteen were the renal type with or without association with osteoporosis.

The technique of reducing the diffusely hypertrophied parathyroid tissue is still being worked upon.

In 1941 Cope reviewed seventy-eight cases, a distinct majority of them the renal type. He, therefore, concluded that the renal complication of hyperparathyroidism is more common than osseous involvement. He further pointed out that any renal tract calcification brings suspicion of hyperparathyroidism and he emphasized the difficulty of distinguishing between primary and secondary hyperparathyroidism.

It is noteworthy that this novel type of hyperparathyroidism had up to then been found only by the Boston group. That this was not due to regional differences was shown by a report recently published from the Mayo Clinic by Keating and Cook. In the twenty-four patients operated upon with the diagnosis of hyperparathyroidism, the classical osseous type was the rarest, 66 per cent having bone changes and 92 per cent renal calculi as a predominant feature. For the diagnosis the decisive factor is the deranged calcium-phosphorus metabolism. In contrast to what had been reported by the Boston group, none of the twenty-four patients had the diffuse hypertrophy of parathyroid tissue as it had been reported there comparatively frequently, and all twenty-four patients had seasonal character is being studied (Ask-Upmark). Neither has the role of topography referred to.

#### THE CLINICAL PICTURE

A classification of the various types of hyperparathyroidism may be made from different viewpoints. According to the symptomatology, Shelling and also Kyser distinguished three groups of symptoms:

- 1 Symptoms due to hypercalcemia
  - a. muscular weakness
  - b. lassitude
  - c. hypotonia
  - d. chronic constipation
  - e. occasionally slow pulse and cardiac arrhythmia (in severe cases tachycardia)
- 2 Symptoms related to the skeletal system
  - a. pain of bones and joints
  - b. cystic regions in the long bones and scalp
  - c. spontaneous fractures
  - d. kyphosis, scoliosis, and deformity of the thorax
  - e. deformities of the long bones
  - f. waddling gait or inability to walk
3. Symptoms due to transportation and excretion of calcium
  - a. polyuria and polydipsia
  - b. enuresis nocturna and dysuria
  - c. renal complications

It shall be shown later that especially the renal symptoms have recently gained particular importance and often dominate the scene.

When describing the development of the disease we will have to deal with the most frequent type of hyperparathyroidism, that more or less progressively developing typical condition referred to by Lièvre as "*forme typique évolutive*" covering the majority of cases of hyperparathyroidism.

However, in attempting a classification both pathogenesis and symptomatology should be taken into account.

#### PRIMARY HYPERPARATHYROIDISM

Let us, first of all, consider the type we should like to describe as primary hyperparathyroidism, falling into the following categories:

1. The classical osseous type caused by the presence of one or two parathyroid adenomas





Biochemically the osseous type of primary hyperparathyroidism is usually quite well defined. Gutman reported, in the 91 out of 114 cases of hypercalcemia he published, distinct and even extreme values of over 120 mg. per 100 c.c. Only if, as it occurs in the late stages of the disease, renal insufficiency supervenes with retention of phosphates does the increase in the serum of calcium disappear. In cases of this kind it is of importance to determine the inorganic phosphorus and the nonprotein nitrogen in order to get a clear idea of the condition.

Since hypercalcemia is also encountered in other bone diseases (multiple myelomas, cancer metastasis), it cannot in itself be regarded a characteristic of hyperparathyroidism.

In the opinion of several authors hypophosphatemia is a reliable guide in the diagnosis of primary hyperparathyroidism. If it occurs together with hypercalcemia, the diagnosis is established. However, in the presence of renal insufficiency the inorganic phosphorus in the serum usually shows a marked increase. Serum phosphatase is high in primary hyperparathyroidism, especially in the ultimate stage (usually 8 to 40 Bodansky units). It is worthy of note that this holds true only of the osseous type of primary hyperparathyroidism (see under renal type). It is in general indicative of decalcification of the skeleton and thus not only characteristic of hyperparathyroidism.

In primary hyperparathyroidism the calcium and phosphorus balance is negative, which means that considerably greater quantities of calcium and phosphorus are eliminated in the urine than would correspond to the calcium and phosphorus intake. As soon as renal insufficiency sets in, the calcium elimination in the urine becomes reduced while greater quantities are eliminated in the feces (Albright, Aub, and Bauer). A negative calcium and phosphorus balance alone is not, however, characteristic of primary hyperparathyroidism.\*

On perusal of the literature it appears that even today, after it has been established by the Boston group that the renal type is steadily increasing, in the international literature the classical type of hyperparathyroidism is the most common.

\*Regarding the various biochemical aspects referred to, it should be pointed out that Jaffe and Bodansky (1943) described as normal calcium values in the serum, fasting values for adults, 9.5 to 10.5, for children, 10.0 to 11.5, for infants, 10.5 to 12.0.

According to Woodard 10 to 11 per cent for adults is normal although values up to 12 mg. per cent have been found in normal individuals.

Jaffe and Bodansky considered a value of at least 11.5 for adults and 12.5 for children as normal. These values are to be understood as the number of milligrams per 100 c.c. of serum.

Normal values for inorganic phosphates are 2.5 to 4.0 mg. per 100 c.c. for adults, 4.5 to 5.5 for children, and 5.5 to 6.5 for infants. A drop to lower than 0.5 below normal level should be considered as indicative of hypophosphatemia, while 1.0 beyond the upper limit indicates hypophosphatemia.

Thus, for example in a review of 135 cases (1936) Wilder and Howell found all of them to belong to the classical osseous type.

**Primary Hyperparathyroidism, Renal Type Caused by Adenoma.** It has already been pointed out that renal complications are likely to appear when hyperparathyroidism persists for some time. However, renal primary hyperparathyroidism is the term applied to that variety which manifests itself first of all by renal symptoms even prior to skeletal changes. This form which is of utmost importance has so far been reported only by a few authors. Cope assumed that the first reaction provoked by parathormone does not occur in the bones, which could be verified in the majority of cases at the Massachusetts General Hospital. According to this author the most common type of hyperparathyroidism is the renal one (calculi) and is explained by the precipitation of calcium in the urinary tract. In 1944 Cope reviewed seventy-eight cases of his own (see Table II).



the calcium level in the serum was no higher than 11.9 mg. per cent, phosphorus 2.9 mg. per cent, and phosphatase 8.1 Bodansky units, while after operation calcium was 8.4 mg. per cent, phosphorus 4.2 mg. per cent, and phosphatase 4.7 Bodansky units. Thus, for example, in a review of 135 cases (1936) Wilder and Howell found all of them to belong to the classical osseous type.

*Primary Hyperparathyroidism, Renal Type Caused by Adenoma.* It has already been pointed out that renal complications are likely to appear when hyperparathyroidism persists for some time. However, renal primary hyperparathyroidism is the term applied to that variety which manifests itself first of all by renal symptoms even prior to skeletal changes. This form which is of utmost importance has so far been reported only by a few authors. Cope assumed that the first reaction provoked by parathormone does not occur in the bones, which could be verified in the majority of cases at the Massachusetts General Hospital. According to this author the most common type of hyperparathyroidism is the renal one (calculi) and is explained by the precipitation of calcium in the urinary tract. In 1944 Cope reviewed seventy-eight cases of his own (See Table II).

The most striking feature of this case appears to be the fact that although the disorder had been present for twenty-five years no typical skeletal involvement was noted. The negative Sulkowitch test was the result of a low calcium diet and it is said to be positive only in connection with a normal calcium intake.

In December, 1945, Keating and Cook of the Mayo Clinic made a very important publication reviewing twenty-four additional cases of hyperparathyroidism. After the authors had adopted the examination and observation methods of the Boston group, they were able to find, during the course of two and one-half years, the previously mentioned twenty-four cases while in the preceding fourteen years a total of only fourteen cases of hyperparathyroidism had been detected at the Mayo Clinic.

These twenty-four cases were grouped by the authors as follows

1. Seven cases, 29 per cent, belonging to the classical skeletal type of hyperparathyroidism. Three of them involved renal calculi and two others calcification of the renal parenchyma.
2. Nine cases, 38 per cent, showing minimal or atypical demineralization of the skeleton. All these patients had or had had renal calculi.
3. Eight cases, 33 per cent, having renal calculi without recognizable skeletal involvement.

Summing up, therefore, bone changes were present in 67 per cent of the cases while in 92 per cent there were either renal calculi or calcification of the kidneys. Fourteen out of the twenty-four patients had previously undergone a total of twenty operations for renal calculi so that it seems justified to search for hyperparathyroidism if a patient reports recurring attacks of calculi (Cope).

The authors concluded by verifying Albright's earlier statement: (1) Hyperparathyroidism is more common than generally supposed; (2) renal involvement is more frequent and diagnostically more important than osseous involvement; (3) every patient who has renal calculi should be suspected of having hyperparathyroidism.

Studying separately the purely renal cases without osseous changes reported by Keating and Cook and Churchill and Cope, as well as by Cope alone, and comparing them with those of the classic type, it is first of all noticed that the biochemical changes are much more pronounced in the classic skeletal variety. This applies in the same measure to the increase of the calcium level of the serum as to the lowering of the phosphorus and the increase of the phosphatase values. Keating and Cook, for example, reported calcium values of less than 12.5 mg. per cent in twelve out of twenty-four cases. Of a greater diagnostic value, although not so distinctive, are the low phosphorus proportions. In the purely renal cases the alkaline phosphatase was normal.

Considering that in the second group, too, the radiograms showed only decalcification or fibrosis of the skeleton as determined by Camp and Ochsner and that in the third group the bones were altogether normal, we should ask ourselves with what degree of certainty the diagnosis of hyperparathyroidism can be established. Thus, operations were for the greatest part performed only on the strength of repeatedly determined slightly changed biochemical values and it should not surprise us that at the same time when the twenty-four patients with hyperparathyroidism were operated upon with positive result, six others underwent operation in which the suspicion of hyperparathyroidism could not be verified. The question is whether it would not be advisable to include still other diagnostic methods as, for example, the chronaxia test or the Hamilton test (Schwartz, see Baine and Rivoire).

In those cases in which operation gave a positive result it was always an adenoma (in one of the cases two) that was found. None of the patients had hyperplasia of all parathyroids, which adds to the value of these findings. In three of the patients the tumor could be palpated prior to operation. In all of them its localization was at the neck and never in the mediastinum.

The divergency between these findings and those reported by Cope (20 per cent of cases with tumors in the mediastinum) is noteworthy.

Microscopically, the renal type of hyperparathyroidism is not distinguished from the classical one by preponderance of any kind of cells in the histologic structure of the adenoma.

Following operation the calcium level always dropped considerably and the phosphorus values returned to normal.

The establishment of a renal type of primary hyperparathyroidism has thus become an important clinical-pathologic fact. Its diagnosis is possible only by careful observation and repeated biochemical examinations. The Sulkowitch test considerably facilitates the diagnosis. By discovering hyperparathyroidism in cases of this kind, although we cannot spare the patient a renal operation, we are probably able in a number of cases to forestall recurrences.

It seems, therefore, opportune to discuss the relationship between *nephrolithiasis* and *hyperparathyroidism*. It has been pointed out that in the classical type of osseous hyperparathyroidism of long standing, lithiasis supervenes and may by way of uremia be responsible for a fatal outcome. I saw this happen in my first case in 1926 and also in 1932. Here lithiasis must be considered the final stage. It has, however, also been observed that calcium were the first sign

of hyperparathyroidism even preceding osseous changes Snapper (1943) commented as follows on the purely renal initial type of hyperparathyroidism:

The human skeleton contains approximately 900 Gm calcium. Even in the presence of a markedly negative calcium balance the daily loss of calcium does not exceed about 0.5 or maximally 1.0 Gm. Thus several months or even years may elapse before changes become apparent in the bones. But this is also the reason why skeletal changes may be preceded by lithiasis owing to the excretion of calcium and phosphorus in the urine.

We are thus confronted with the question as to whether by abolishing the state of hyperparathyroidism, that is, by removing a parathyroid adenoma, we are in a position to forestall the further formation of renal calculi and to reduce the number of relapses after operation for calculi

Naturally, recurrences after operations for calculi have been reduced with advancing technique In 1915 Cabot and Crabtree reported 56 per cent of recurrences after nephrotomy and 51 per cent after pyelotomy. In 1922 Barney reported 32 per cent for the same hospital By 1924 the number of recurrences at the Mayo Clinic (Braasch and Foulds) had been lowered to 10.79 per cent. Other authors listed 14.9 per cent, after pyelotomy, 32 per cent after pyelonephrotomy, and 29.4 per cent after nephrotomy (1937). A synopsis of results was given by Clement in 1940 As a matter of course, only part of these cases can be attributed to hyperparathyroidism since infection, stasis, operative trauma, and other unknown sustained traumas certainly play an important role although we do not know to what extent

However, in 1934, attention began to concentrate on the relationship between renal calculi and hyperparathyroidism. Barney and Mintz pointed out that in 4 to 5 per cent of cases hyperparathyroidism plays an important etiologic role in lithiasis Griffin, Osterberg, and Braasch attribute only 0.2 per cent of their cases of renal calculi to hyperparathyroidism, based on biochemical examinations of 1,026 patients Cope reported 10 to 15 per cent According to Keating and Cook cases of renal calculi caused by hyperparathyroidism constitute but 2 per cent of the total for the period during which they studied renal hyperparathyroidism Snapper pointed out that in Amsterdam oxalate stones are much more frequent than calcium phosphate stones None of his patients with recurrent stone attacks, however, presented hypercalcemia or hypercalciuria.

My experience at a hospital in Palestine where, as everywhere in the Near East, renal lithiasis is extraordinarily common was a similar one For a long time we have tried in vain, lately by means of the Sulkowitch test, to establish hypercalciuria in recurrent renal calculi, recurrences occurring here in Palestine after operation in 20 per cent of cases None of the cases so far yielded the least indication, in history, clinically as well as biochemically, of hyperparathyroidism In some cases the Sulkowitch test was slightly positive, but subsequent biochemical examinations (Ca, P) revealed nothing pathologic

In only one autopsy made on a patient who had suffered from calculi and had been operated upon in my department was a parathyroid adenoma detected.

## CASE REPORT

The history was that of a man 45 years of age at the time of his death. He came to Palestine five years before and soon afterward he experienced urinary trouble for the first time. The symptoms were typical of stones in the kidney and bladder. About two years before he had been operated upon, stones being removed from the left kidney by nephrotomy and from the urinary bladder by a scietio alta. After the operation the patient felt well up to two months before death.

He then had an attack of renal colic on the right side, which was the side not operated upon. A roentgenogram was taken which revealed the presence of large stones in the right, smaller ones in the left kidney.

A right nephrotomy was performed and a large stone removed which had broken up into three fragments. The chemical laboratory reported that the stones were composed chiefly of ammonium magnesium phosphate.

The patient seemed to recover satisfactorily until an apparently latent intestinal infection (bacillary dysentery) manifested itself on the fifth day after operation. From that time on rise in temperature, diarrhea, and collapse caused a steady downward course for the next seven days until the death of the patient.

An autopsy was performed. Necrotizing colitis and bronchopneumonia with abscess formation were established as the cause of death.

The most interesting findings were those in the cervical region. The thyroid gland appeared normal except for a small adenoma in the right lobe and moderate enlargement of the pyramidal lobe. Near the right lower pole of the gland an oval nodule was discovered connected with the thyroid gland by a stalk which was composed of blood vessels and fat tissue.

On histologic examination the described node proved to be composed of parathyroid tissue. There were no fat or oxyphil cells present as might be expected in view of the patient's age. The node was composed mainly of chief cells and of the so-called water clear cells.

It was decided that this was a true adenoma of parathyroid tissue, and, therefore, most likely primary hyperparathyroidism, apart from histologic considerations, mainly for two reasons:

1. The size of the parathyroid nodule was much larger than ever seen in cases of secondary hyperplasia of the parathyroids encountered in different conditions of the skeleton as well as in chronic nephritic lesions.

2. There was no enlargement of the rest of the parathyroid tissue which should be expected in case of secondary involvement of the glands.\*

The x ray picture of the lumbar spine, the pelvis, and the hip region was negative.

In Vienna, where I used to work, I explored the neck region operatively and searched for a parathyroid adenoma in two cases of recurrent renal calculi (Mandl, 1938). Biochemically there was no indication of hyperparathyroidism and the bones were also normal. I am unable to give exact details of the one case. I have been in communication with the second patient, who now lives in New York.

The history of this patient, who had been in a German concentration camp where he had been kicked in both sides and sustained a renal hemorrhage, told of renal calculi in both kidneys later in 1936. The stones consisted of calcium and phosphate. On operation neither a parathyroid adenoma nor hypertrophy of the parathyroids was found. Therefore, after it was concluded that there were actually four normal parathyroid glands, two of them were removed. Four years after this operation the patient wrote from New York that he had become worse, had frequent colics, and was thus incapable of attending to his business and was confined to bed.

\*I am obliged to Dr. Ungar of the histology laboratory for kindly placing this autopsy record at my disposal.

Radiograms taken at this time, compared with earlier ones, showed marked increase of bone formation in both kidneys. The stones were now and then expelled with or occasionally even without colic. According to latest results of examinations the renal function was nevertheless satisfactory. An acid diet was prescribed for the patient and he was advised strictly to avoid calcium and phosphates. The kidney pelvis was irrigated with trypanflavine. Acidification of the urine proved difficult. He had often been advised to submit to operation but this operation had never been performed.

In Vienna the findings had been as follows: Serum calcium 10.8 mg. per cent; phosphorus 2.95 mg per cent; calcium in the urine 105.6 mg per cent, phosphorus in the urine 0.8 mg. From New York the following data were received: creatinine 1.04; nonprotein nitrogen 30.6; calcium 11.2; phosphorus 2.84; total protein 6.04; phosphates 2.4. Since 1942 nothing further has been heard.

The relationship between renal calculi and hyperparathyroidism is of extraordinary importance and in the future the detection of primary hyperparathyroidism in a greater number of cases may possibly help to an appreciable extent to avoid the recurrence of calculi. However, it would be of even greater importance to forestall a further osseous development by an early diagnosis and early institution of treatment of hyperparathyroidism.

It must be mentioned, that, apart from calculi caused by hypercalcemia and hypercalciuria, these pathologic changes may also be responsible for the precipitation of calcium in the renal parenchyma (nephrocalcinosis). Cases of this kind have been described and collected from the literature by Albright, Braid, Cope, and Bloomberg. Those published after 1934 have been reviewed by Snapper (1943).

*The Gastrointestinal Type of Primary Hyperparathyroidism Caused by Adenoma or Hyperplasia of the Parathyroids*—It is not yet certain whether there exists a gastrointestinal type of hyperparathyroidism similar, for example, to the renal type in which the other classical manifestations are pushed to the background and gastrointestinal symptoms dominate the scene. Lièvre (1932) was the first to describe a variety of hyperparathyroidism with severe gastrointestinal manifestations which he witnessed in two of his patients who, however, otherwise had the classical osseous type. In both, a parathyroid adenoma was removed with good result.

In Lièvre's second case there were major crises at intervals of about a fortnight during which the patient, under constant vomiting, was intolerant to any kind of food.

Lièvre's third patient also developed *crises gastriques* recurring every two, three, or four weeks characterized by vomiting and painful abdominal colic. This patient, however, also had classical osseous hyperparathyroidism with parathyroid adenoma.

Similar cases have been described by Hunter, Pemberton, and Geddie, Barr, Bulger, and Dixon. One reported by Ask-Upmark included considerable congestion and retention of the gastric contents when a roentgen examination was made because of gastric symptoms accompanying hyperparathyroidism. However, all cases outlined here were of the classic type associated with gastrointestinal manifestations.

A different condition is that referred to by Morelle. His patient had been admitted to the hospital with intestinal obstruction and all signs of ileus.



The calcium level of the serum was 19.7 mg. per cent. After this had been established, an examination was made of the skeleton where, however, only moderate decalcification was found. Since vomiting increased in intensity, the neck region was explored operatively and a parathyroid adenoma detected. After operation the patient rapidly recovered and all symptoms disappeared.

Snapper (1943) quoted from the Dutch literature a similar case reported upon by Beyerink. Here, too, the condition was clinically characterized by attacks of vomiting. Calcium in the serum was 19.3 to 21.0 mg. per cent; phosphorus 2.0 to 2.5 mg. per cent. X-ray findings were normal.

The skeleton and kidneys being normal, the two cases must be considered as typical gastrointestinal types of hyperparathyroidism.

Renewed attention has recently been drawn to this form of hyperparathyroidism by Rogers, who described two patients having a rather acute course. In both, autopsy revealed duodenal ulcer. These two cases are interesting because of the overlapping of the two diagnoses, ulcer and hyperparathyroidism (Gutman and Parsons), and further because of the fact that in hyperparathyroidism a diet rich in calcium and phosphorus as it is prescribed for ulcer may aggravate the general symptoms of hyperparathyroidism. The danger of this diet in the presence of hyperparathyroidism has also been emphasized by Hunter and Auli, Albright, Bauer, Claflin, and Cockrill.

In one of Rogers' two cases, both aggravated by ulcer diet, an adenoma and in the other primary hyperplasia of the parathyroid glands was found.

*Primary Hyperplasia of all Parathyroid Glands With Osseous, Renal or Gastrointestinal Involvement.*—The whole concept of hyperparathyroidism, implying a rejection of the idea of a compensatory parathyroid hyperfunction in certain osseous diseases, has become confused by the fact that there may also be a primary diffuse hyperplasia of all parathyroid glands creating a clinical picture exactly similar to that caused by isolated adenomas. The same applies to the presence of two or several adenomas. Even before 1934, when Albright, Bloomberg, Castleman, and Churchill were the first to refer to three cases of this type particularly, autopsy records had been made available in which osteitis fibrosa generalisata was associated with multiple adenomas or enlargement of all parathyroid glands (Schmorl, Molinens, Hoffheinz, Goedel, Paul, Bergstrand, and Hanke).

There was also reference to two operations: Hellström, in 1931 after having removed one parathyroid adenoma without success, on the occasion of a second operation found another one, the removal of which effected definite cure. In a case published by Hunter in 1931, operation revealed two normal parathyroid glands but also two adenomas which could be removed while the normal organs were left untouched. A similar case was described by Abel. The clinical aspect of all these cases was that of the classic osseous hyperparathyroidism (see Albright and associates, 1934).

However, the cases published by Albright and co-workers in 1934 with hyperplasia of all parathyroid glands presented quite a new picture, markedly different from that known up to then. The outstanding feature of these cases,

as it appeared, was the association of hyperplasia of the entire parathyroid tissue with the renal form of hyperparathyroidism in the absence of any sign of osseous involvement. This alone at first let it appear justified to speak of a separate variety of the disease. As a causative factor at that time an underlying pituitary disorder was suggested stimulating the function of the entire parathyroid system so that more hormone was produced than required by the organism. It was pointed out that histologically the cases were characterized by an increase of the water-clear cells in contrast to the increase in the number of chief cells as it occurs in ordinary adenomas. This hyperplasia of the entire parathyroid system was later corroborated by others although with certain restrictions. At the Massachusetts General Hospital, in 1944, Cope found among his seventy-eight patients with hyperparathyroidism seven with hyperplasia of all four parathyroid glands, an occurrence that has been compared to a general hyperplasia of the thyroid tissue in hyperthyroidism.

On the other hand, in 1944 Cope pointed out that the clinical picture of diffuse parathyroid hyperplasia was in no way different from that of isolated parathyroid adenomas since all characteristics arising from the presence of an adenoma were also encountered in diffuse hyperplasia (osseous and renal type).

Regarding the cause of this hyperplasia, Cope was unable to furnish further information beyond the fact that the search for disturbances in the pituitary function had been in vain.

The histologic picture described by Cope, however, was the same as that referred to by Albright and co-workers in 1934: hyperplasia and hypertrophy of the water-clear cells which occasionally had assumed sixty times their original size.

Cope pointed out that at operation these changes are easily recognizable but he recommended, nevertheless, making frozen sections during the operation in order to establish the diagnosis beyond any doubt.

It might be assumed that owing to the preponderance of the renal type of the disease diffuse hyperplasia should be very common. This could not, however, be verified by the studies performed at the Mayo Clinic. Here the twenty-four cases reported upon by Keating and Cook (1945) included twenty-three cases of isolated and one of multiple adenoma while none of them involved primary hypertrophy of the entire parathyroid tissue. It should be recalled that the cases referred to by these authors were predominantly of the primary renal type or at least of secondary lithiasis. It was not before 1946 that Rogers gave an account of the first case of primary hyperplasia of the parathyroid glands observed at the Mayo Clinic. This was one of the cases with gastrointestinal manifestations and association with duodenal ulcer. Here, too, the water-clear cells were encountered.

Summing up, it may, therefore, be said that diffuse primary hyperplasia of the parathyroid tissue is much less common than isolated adenomas (Lage and Greene, 1943). Its clinical manifestations are the same as those provoked by isolated adenoma (osseous, renal, and gastrointestinal form). The cause

of this diffuse hyperplasia, although of greatest etiologic interest, is as yet imperfectly understood. The cell type characteristic of diffuse primary hyperplasia of the parathyroid tissue is that of the water-clear cells described by Getzova.

#### PRIMARY AND SECONDARY HYPERPARATHYROIDISM

A short historical review may precede the discussion of this important question. In 1907, when Erdheim published the important results of his studies on parathyroid "hyperplasia," at first no difference was made by pathologists between enlargement, hyperplasia, adenoma, or tumor of the glands. The condition was generally referred to as hyperplasia and Erdheim himself (1907) mentioned it in his report of three cases of osteomalacia. But there was also reference to a "tumor" 3.6 by 2.0 cm. in diameter. Whether a clear distinction was at that time made between osteomalacia and osteitis fibrosa generalisata is not clear. Hyperplasia of this kind was, however, noted by Erdheim and others in osteomalacia as well as in rickets, in men and in rats where it had been produced experimentally. These observations which were then even extended to Recklinghausen's disease formed the basis of Erdheim's theory, implying that hyperplasia was here the result of the decalcification of bones and, therefore, of a compensatory nature. Larger quantities of hormone would be produced, warranting the normal ossification of the bones, and decalcification was halted.

When after the first successful parathyroidectomy a decisive therapeutic effect was noted I defined my opinion regarding the theory of this operation as follows (Mandl, 1926):

Important objections have been made against Erdheim's theory which followed as a logical conclusion from his basic experimental studies. First of all, it seemed odd that the supposed hyperplasia, considered a compensatory hypertrophy by Erdheim, should in the vast majority of cases be found only in one instead of several or all parathyroid glands. Hoffheins found no more than four cases, i.e., 15 per cent, in the literature in which enlargement was reported for more than one of the glands; and 85 per cent, therefore, presented involvement of no more than one of them. Erdheim defended his opinion by pointing out that enlargement of one single gland was sufficient to meet the exaggerated functional requirements. This explanation should, in my opinion, be rejected since actually the enlargement of one single gland is by no means able to control the calcium metabolism in a way that no pathological manifestations would arise. On the contrary, we know from observation and from post mortem studies on individuals who died from osteitis fibrosa generalisata that in spite of enlargement of one parathyroid gland their calcium metabolism had been completely deranged. It is equally impossible to presume that nature which usually provides so generously for the compensation of an abolished function should not make use, in an emergency, of the vast reservoir of the three remaining normal parathyroid glands. It might further be pointed out that in several cases the parathyroid enlargement definitely presented the character of a new growth. Genuine new growth, however, can by no means be considered a compensatory action for an abolished function."

The successful extirpation of the parathyroid adenoma seems to have verified my opinion.

On the other hand, Snapper was right when he pointed out that in view of the results of the first parathyroidectomy for Recklinghausen's disease the entire problem seemed simplified. Today it is generally known that in fact this only seemed so, and a general rejection of the idea of a compensatory secondary hyperparathyroidism is no longer justified.

It is a generally established fact, verified by experience from all over the globe, that Recklinghausen's and other diseases are no doubt caused by primary hyperparathyroidism, which means that in the vast majority of cases one or two parathyroid adenomas or diffuse hyperplasia of the entire parathyroid tissue is the responsible causative factor. However, what cases develop adenomas and when hyperplasia of the parathyroid tissue occurs are not yet understood although there is no longer any question regarding their causative nature.

On the other hand, Erdheim's theory has regained its validity for that type of case which on the strength of experimental and clinical studies must be considered a secondary hyperparathyroidism.

This experimental secondary hyperfunction of the parathyroids can be provoked in various ways, by D avitaminosis as well as by withholding ultraviolet rays from chickens, decalcification of bones and parathyroid hyperplasia were obtained (Doyle, Nonidez and Goodald, Higgins and Sheard, Sheard, Higgins and Wilder). The parathyroids grew to ten times their normal weight. Addition of cod liver oil, irradiation with ultraviolet rays, or administration of parathormone prevented this hyperplasia.

According to Oberling and Guerin, by raising chickens in the dark or by withdrawing calcium from their diet, parathyroid hyperplasia can be produced and is due to proliferation of the water-clear cells.

By means of a biliary fistula and a consequently disturbed absorption of fat, Duttman, Tamman, Dieterich, and Loewy were able to effect decalcification and secondary hyperplasia of the parathyroids (see Snapper, 1943).

From a clinical viewpoint it should be emphasized that even today the parathyroid hypertrophy existing in osteomalacia is, in accordance with Erdheim's findings, regarded as a secondary manifestation.

Further, multiple myeloma may occasionally effect secondary parathyroid hypertrophy. These myelomas cause decalcification of bones so that hypercalcemia and hypercalciuria may develop and the picture of Recklinghausen's disease thus may be simulated. Cases of this kind have been referred to repeatedly in the literature. However, none of Snapper's nine patients showed increased calcium values in the blood. It is not particularly surprising that in the presence of myelomatosis, as soon as renal insufficiency supervenes, the phosphorus in the serum rises. Conditions are here similar to those prevailing in primary hyperparathyroidism. Regarding differential diagnosis, Snapper pointed out that in myelomatosis the serum phosphatase values are not increased. It must be admitted, however, that secondary parathyroid hyperplasia developing as a result of these biochemical changes is rare and that it is by no means a characteristic of this disease. However, this kind of secondary hyperplasia

has, for example, been referred to by Barr, Bulger, and Dixon. Similar findings have been reported by Piney and Raach.

In extensive carcinomatous bone metastases, as a consequence of malignant disease of the bone, the destruction of the skeleton is similar to that of the previously mentioned disorder. Occasionally hypercalcemia and hypercalcemia may also develop. I have seen two cases of this kind in which, however, autopsy revealed no hyperplasia of parathyroid tissue. Important data regarding that point have, however, been published by others. Thus, for example, Mason and Warren gave an account of a patient on whom an operation had been performed for mammary carcinoma five years earlier. The radiogram showed carcinosis of the entire skeleton. Nevertheless, the neck region was explored operatively and metastases were detected in the thyroid and parathyroid. In these authors' opinion the marked degree of hypercalcemia in this case either was connected with an associated hyperparathyroidism or, on the other hand, was due to the extensive destruction of bones. I am inclined to share the latter assumption as being the more probable one.

An exceptional case is that reported by Klemperer since this author was the only one to detect a parathyroid adenoma instead of diffuse hyperplasia of all parathyroids secondary to bone metastases after mammary carcinoma. Destruction of the bone tissue was complete and had in Klemperer's opinion been responsible for the formation of one isolated parathyroid adenoma. As I pointed out in 1926, compensatory hypertrophy is conceivable only if it involves the entire parathyroid tissue and it appears that here, in accordance with Snapper's view, we are dealing with a "mild degree of Recklinghausen's disease with a parathyroid tumor" in addition to extensive bone metastases after mammary carcinoma.

The following case described by Ben-Asher (1939), therefore, represents a logical development.

A man 58 years of age was admitted to the hospital with vague complaints. Radiography revealed a large multilocular cyst of the right humerus, while the skull showed multiple areas of rarefaction. A similar picture was found in the bones of the pelvis, the right femur, and both fibulae. Although everything pointed in a direction of bone metastases, hyperparathyroidism could not be excluded. Continuous examinations after a test diet revealed persistent hypercalcemia and low phosphorus levels in the blood in addition to hypercalcemia. Therefore, an operation was performed and at the right side of the neck two markedly enlarged parathyroids were found and removed. Although the patient survived the operation the calcium level of the blood remained unchanged. Since the condition was not improved, a second operation was done in order to detect similar changes on the left side of the neck, but without result. Ten months later the patient died, no autopsy was made.

The case was one of secondary hypertrophy of the parathyroid, the removal of which, therefore, was unlikely to effect improvement.

The cases outlined in the foregoing are more interesting in a differential-diagnostic respect than regarding the secondary hyperparathyroidism which may occasionally appear in such cases.

More important and frequent are those cases which today dominate the field of secondary hyperparathyroidism, in which either in children or in



Radiographically the bones were normal; there was neither decalcification nor deformity. The "dwarfism" consisted in retarded growth (122 cm. instead of 157 cm.) and deficient weight (22.5 kg. instead of 40 kg.)

The synopsis given in Table IV seems important from a practical viewpoint illustrating the main differences between primary and secondary hyperparathyroidism.

In a diagnostic respect conditions are not so simple as it would seem from Table IV, owing to the fact that in primary and also in secondary hyperparathyroidism, in the former especially as a result of latest studies, the main character of the disease so frequently holds the foreground. If a patient suffering from hyperparathyroidism caused by parathyroid adenoma is to develop renal insufficiency at a comparatively early stage which in turn may stimulate an even more pronounced hyperfunction in the parathyroids. In this way the degree of hyperparathyroidism may not only become intensified but the difference between primary and secondary parathyroid hyperfunction may become blurred. (On the other hand as pointed out by Jaffe, in a case such as one of secondary hyperparathyroidism subsequent to renal disease, the parathyroid hyperfunction may become so excessive that it exerts a marked action on bones as well as on the already existing renal insufficiency. Here further studies are of no great avail as it is seen, for example, in a case reported by Cope in 1944

A man, aged 65 years, entered the hospital April 27, 1947, to receive radiotherapy to a basal cell carcinoma of the scalp. He had additional complaints; first hyper-

TABLE IV

PRIMARY HYPERPARATHYROIDISM	SECONDARY HYPERPARATHYROIDISM
<i>Clinical Type</i>	
Osteous	Osteous (osteomalacia, rickets, etc.)
Renal	Renal (congenital lesion, hypoplasia or glomerulonephritis, renal failure or anemous); renal form in chronic adolescents, rare in adults
Gastrointestinal, only a little	
<i>Biochemical Findings</i>	
Marked hypercalcemia	Hypocalcemia
Inorganic phosphorus in serum low	Inorganic phosphorus high
Phosphatase high	Phosphatase high
<i>Bones</i>	
Spontaneous fractures frequent	Fractures very rare but if present bones frequent
<i>Radiography</i>	
Cysts and tumors	Porosis or fibrosis
<i>Parathyroid Findings</i>	
Usually one, rarely two adenomas, hyperplasia rare	Only hyperplasia
<i>Histology</i>	
Adenoma: various cell types usually chief cell adenoma	Chief cell and
Primary hyperplasia: mostly water-clear cells	
<i>Operation</i>	
Early operation indicated	Operation

one and one half years weakness, especially of the legs, had been progressive, and for the previous few months the patient had been bedridden. Neurological study showed no reason for the weakness.

Lateral roentgenogram of the skull showed diffuse small rarified areas. Spine and pelvis were diffusely decalcified with a single cystlike area in the second lumbar vertebra and another in the crest of the ileum. Diagnosis was multiple myeloma.

Chemical findings revealed no Bence Jones protein and no elevated serum protein as would be expected in multiple myeloma. Blood serum calcium level was 11.2 per cent, serum phosphorus 5.3 per cent, and phosphatase 17.1 Bodansky units. There was a moderate amount of calcium in the urine and intermittent albumin. Serum protein was 5.4 Gm, nonprotein nitrogen 29 mg., and uric acid 6.6 mg.

A tentative diagnosis of primary hyperparathyroidism with secondary impairment of the renal function was made. Upon repeated examinations, calcium and phosphorus values were practically unchanged. The phosphatase rose further to 19 to 22.5 units. Later roentgenograms showed decalcification of the bones of the extremities. The medical service decided that the patient probably had primary renal disease with secondary hyperparathyroidism. The surgical service on the other hand, judged the hyperparathyroidism to be primary, basing the decision on the slightly elevated serum calcium level (11.3 mg at the highest). Had the parathyroid overactivity been initiated by the phosphate retention, the calcium level should still have been below normal. Operation was not advisable, however, since the renal disease had progressed to such an extent that some degree of hyperparathyroidism was thought necessary to maintain the calcium level.

The elevated phosphate level would depress the calcium once a tumor was removed and the other parathyroid glands would undergo secondary hyperplasia. One form of hyperparathyroidism would be exchanged for another.

After discharge, the patient entered the hospital again on May 15, 1942, with a diagnosis of pyelonephritis to which he succumbed on June 6, 1942.

At post mortem examination, an encapsulated adenoma of the right upper parathyroid was found, measuring 22 by 6 mm and weighing 24 gm. The three other glands were normal. Giant cell tumors and cysts were found. There was decalcification of the ribs. The kidney parenchyma had been severely damaged. There was calcification of the lungs.

This patient illustrated the difficulty of making a diagnosis between primary and secondary hyperparathyroidism in the presence of impaired renal function.

The post-mortem findings proved that the primary form of the disease was present since he had an adenoma of the parathyroid and three uninvolved glands.

Although there is today no longer any doubt as to the existence of a secondary type of hyperparathyroidism, it should be borne in mind that it is extraordinarily rare and should be taken into account especially if the leading feature of the clinical picture is renal disease (setting aside the destructive bone diseases referred to previously).

#### CASES OF HYPERPARATHYROIDISM WITH SPECIAL CLINICAL FEATURES

Mention should be made of the fact that hyperparathyroidism may run an extremely protracted course and parathyroid tumors may be present without provoking any clinical manifestations while, on the other hand, there is a very acute toxic type of hyperparathyroidism that may very soon become fatal. These are the two extremes but are both of great importance.

*Silent or Inactive Tumors of Parathyroids.*—Cases of this kind listed in the literature up to the year 1932 have been collected by Lièvre with addition of one



of his own cases. These cases were reported upon by Léri, Faure, Beaulieu and Ruppe, Léri and Lanopier, Pareira and De Castro Freire, Hirsch, and Willich. The latter gave an account of the case of a woman 56 years of age who had had symptoms for twenty-six years, after which spontaneous cure occurred. Since then cases of this kind have again and again been reported. Thus, for example, Keynes performed an operation in a 50-year-old woman on a hard swelling of the left side of the neck, removing the growth, which showed no attachment to neighboring organs. The tumor weighed 18 Gm and had, histologically, a normal parathyroid structure consisting exclusively of oxyphil cells. Radiograms of the skeleton made after the operation revealed nothing of importance. Keynes thought he was dealing with an inactive parathyroid tumor.

Barker and Brines described the case of an 18-year-old girl who had complained of abdominal symptoms and on whom an appendectomy was performed. The authors subsequently removed a tumor, 2.5 cm in diameter, at the level of the cricoid cartilage. The microscopic diagnosis was hyperfunctioning parathyroid adenoma.

Röntgenograms taken later showed, in various parts of the skeleton, fine granular mottling even leading to cyst formation in four sites. Another roentgenogram taken seven months later showed that the cysts had vanished.

Spontaneous cure of osseous hyperparathyroidism was reported by Oestling. Occasionally after a period of apparent remission the process may resume its progressive character and become fatal (Linden).

In Colburn's case the patient, after sixteen years of suffering from symptoms indicative of hyperparathyroidism, developed—in the author's opinion, owing to the fact that the disease was not recognized—a tumor in which the operation, although it was done late, nevertheless was done in time. The tumor was found in the mediastinum. The case had been of the osseous and renal type.

*Acute toxic and Cachectic Types of Hyperparathyroidism.*—Even Lièvre in his monograph referred to a *forme cachectique de l'ostéose parathyroïdienne*, adding several examples. At a comparatively early time (1931) such a case was described by Bergstrand.

Two similar cases of this *forme cachectique* were described by Wanke (1930). His first patient died within six months after treatment by curettage for localized osteitis fibrosa which had been localized four years previously. On autopsy, osteitis fibrosa generalisata was found in addition to a parathyroid tumor of a benign type. In this as well as in his second case, in which no operation was performed but which under the signs of progressive cachexia led to a fatal outcome, the microscopic findings were of a parathyroid tumor consisting of chief cells.

Even in the operative era when the recognition of the disease had become more general, interesting cases of acute hyperparathyroidism were reported. The first was that of Lowenburg and Ginsburg (1932) in which acute hyperparathyroidism developed following the administration, by error, of 100 units of parathormone. On the second day the 5-year-old boy became listless and started vomiting. On the fourth day he developed severe mental depression with

high temperature and tachycardia. On the sixth day the mistake was discovered and he improved rapidly. At that time calcium in the blood serum was 19.6 mg.

Another case of acute hyperparathyroidism quoted in the literature is that by Hanes. Whether or not the diagnosis was justified here is doubtful in view of the fact that the patient had had the signs of hyperparathyroidism for five years with typical osseous changes and metastatic renal calcification. When he was prepared for operation he became progressively weaker, began to have a fever, and died before the operation had been performed. On autopsy, a parathyroid adenoma was found in addition to extensive calcification of connective tissue, especially in the kidneys and myocardium, and to a lesser extent in the lungs and stomach. With reference to this case, Albright pointed out that the acute toxic condition develops after the blood calcium has exceeded a certain limit. This is accompanied by a simultaneous rise of the phosphorus values (while they usually drop in typical hyperparathyroidism) "because phosphorus is no longer diffusible at very high levels of calcium." According to that author, therefore, the alarming symptom is not the high calcium level in the blood but rather the abnormally high phosphorus. It should be borne in mind, however, that even in the presence of extremely high calcium values the simultaneous rise of the blood phosphorus is by no means a common occurrence. Even in the presence of as high a value as 23 mg per cent (as reported by Snapper) or even 30 mg per cent (Cutler and Owen), phosphorus values remained low. In Snapper's opinion, it is only in the terminal stage with supervening uremia, owing to renal calculi or renal calcification, that the phosphorus values may also reach excessive proportions. It appears, therefore, that once this stage is attained the suitable moment for operation has been missed.

In 1939, Oliver gave an account of two cases of acute hyperparathyroidism with fatal outcome. The leading symptoms were of a mental and gastrointestinal nature (vomiting, constipation, and anorexia). Later the temperature became elevated, and tachycardia and high urea values supervened.

A similar case was reported upon by Smith and Cooke (1940). The patient had been suffering from a bone disease for two years. Later gastrointestinal symptoms, tachycardia, and rise of temperature suddenly supervened. The patient eventually died under the signs of uremia. Autopsy showed an adenoma composed of chief cells.

Alexander, Pemberton, Kepler, and Broders described another case of this acute type, the patient succumbing within six months.

The next case of acute hyperparathyroidism was that reported by McClure and Lam in 1943, as follows.

Four months before the patient was admitted to the hospital, November, 1931, violent sneezing elicited a tearing sensation in the right side. Just before admission she had dyspnea, weakness, and anorexia. Examination revealed exudation at the base of the right lung, the cellular character of which was suggestive of malignancy, and a roentgenogram of the right femur also aroused the suspicion of a malignant process. After having received deep roentgen therapy, the patient was discharged on Dec. 2, 1931, but had to be readmitted on December 26, because of vomiting and anorexia. When she was again discharged a few days later, she sustained a spontaneous fracture of the left femur.

When she returned to the hospital, the calcium level of the blood was 14.3 mg. per cent and phosphorus 2.57 mg. per cent. Vomiting increased in intensity and the blood calcium rose to 19.4 mg. per cent, phosphorus to 3.83 mg. per cent. On January 20 her mental status was referred to as very cloudy. On February 13, calcium was 14.2 mg. per cent and phosphorus 6.25 mg. per cent. On February 15, the patient died.

Autopsy revealed diffuse hyperplasia of all parathyroid glands. There were further calcium deposits in the lungs, kidneys, and blood vessels. The bone picture was characteristic of an advanced stage of osteitis fibrosa cystica.

The authors were correct when they asked why hyperparathyroidism had not been suspected at an earlier stage.

Eventually, there are two further fairly acute cases reported upon by Rogers for which post-mortem findings are available and both of which involved acute intoxication.

On the whole, therefore, it appears that in a relatively large number of cases the diagnosis of hyperparathyroidism is not considered until it is too late. In my opinion, it would be advisable to perform the simple and inexpensive Sulkowitch test as a routine measure which would reveal any suggestion of hyperparathyroidism without delay. In a greater number of the cases outlined in the foregoing discussion, no calcium and phosphorus determinations had been made.

Mention has been made of the microscopic findings in the less active as well as in the more acute types of hyperparathyroidism in order to show that neither the size nor the cell character has any bearing on the clinical picture.

#### MALIGNANT PARATHYROID TUMORS

Those cases in which hyperparathyroidism is due to malignant tumors deserve separate mention.

In the past few years two papers have appeared dealing in a comprehensive manner with that point (Gentile, Skinner, and Ashburn, Alexander, Pemberton, Kepler, and Broders). First of all it was surprising that of the fourteen cases of Alexander and co-workers, thirteen of them, or 92.8 per cent, were referred to as malignant, while in the large series of Cope, for example, including fifty-eight cases, there was not one case of malignancy.

Apparently the classification is a purely microscopic one and the clinical picture need not always show malignant features.

In any event, the point is important enough to be dealt with in detail. Above all, for purely empirical reasons the parathyroid tumors (eight cases) described by Kocher in 1908, which were characterized by containing glycogen, should either be eliminated, from these considerations or be regarded as "not functioning malignant parathyroid tumors." Later, in 1907, Langhans published reports on four cases with tumors which he considered to originate from the parathyroids, while Harbitz thought them connected with the thyroid gland. Similar reports have been made by De Quervain, Roffo and Landivar, Fasiani, but in none of them, characteristically, is reference made to bone changes. In two cases of this type (Ferrero and Sacerdote, Alessandri) bone metastases contained parathyroid tissue and, in Alessandri's case, parathyroid along with

thyroid tissue. Other publications were made by Hendrich, Guy, Toland, Price and Mowatt, Hall and Choffin, and Armstrong. In none of the cases were indications of hyperparathyroidism found and from a purely clinical viewpoint the tumors were in no way distinguishable from those originating from the thyroid gland.

I performed an operation for a tumor of this category in 1944:

The patient was a woman 46 years of age whose father and brother had had intestinal carcinoma. The patient herself had had a goiter for many years and, especially during the past three years, had suffered from dysphagia and dyspnea. X-ray examination showed a substernal tumor on the left side displacing the trachea to the right. The basal metabolism rate was +11 per cent. On operation, an adenoma was found attached to the left lobe of the thyroid gland, the size of an orange, extending into the sub-sternal space and slightly attached to the esophagus. The tumor was enucleated and resected. Postoperatively there was nothing of importance.

Microscopy showed a malignant tumor containing parathyroid tissue.

In view of the result of the microscopic examination roentgenograms were made of the patient but no skeletal changes could be ascertained and the biochemical findings were likewise negative.

Follow-up examination in 1946 showed the patient in perfect health and without any complaints.

On perusal of the literature referring to these "nonfunctioning malignant tumors of the parathyroid" one finds a total of twenty four cases reported upon until 1945. Clinical signs of malignancy, that is, the appearance of metastases, are referred to by De Quervain, Guye, Toland, Price and Mowatt, and Hall and Choffin. Follow-up examinations, where they could be performed, had usually an unfavorable result. Although, therefore, the tumors were of a very malignant nature, they did not offer the symptoms of hyperparathyroidism.

The first case of malignant tumor which did offer the symptoms of hyperparathyroidism or "functioning malignant tumor of the parathyroid" was reported upon by Wilder and Wellbrock in 1929 and was then included in the study by Alexander and co-workers. These authors also collected the other cases of this type given by Quick and Hunsberger, Sainton and Millot, Snell and Mayo, Petersma, Meyer, Rosi, and Ragins, Gentile, Skinner, and Ashburn, adding, as already mentioned, thirteen of their own cases of malignant hyperfunctioning parathyroid tumors. Meyer and Ragins published another case in 1943.

It seems worth while to subject the clinical picture as well as the development and the microscopic findings to a closer analysis.

Among the thirteen cases of Alexander, Pemberton, Kepler, and Broders, ten are referred to as malignant functioning parathyroid tumors (parathyroid adenocarcinoma grade 1, Broder's classification) and two as adenocarcinoma of the parathyroid gland, grade 3. As far as clinical data are available, neither local recurrences nor distant metastases were noted in any of the cases during the time of observation. Clinically, therefore, there was no indication of malignancy.

From a practical viewpoint the cases given by Gentile, Skinner, and Ashburn and by Meyer and Ragins are of special interest since here recurrences were accompanied by a re-appearance of hyperparathyroidism which, however, dis-

appeared again as soon as they were removed. Possibly similar cases of recurrent hyperparathyroidism are also due to malignancy.

Although the classification introduced by Alexander and co workers promised to throw new light on our knowledge of hyperparathyroidism, it must be pointed out that the clinical development of these and other cases was only very rarely indicative of carcinoma. This is in accordance with the experience that hyperfunctioning endocrine organs in general only exceptionally develop malignant tumors.

From a practical viewpoint, therefore, clinical malignancy does not so far seem to play any important role in connection with hyperparathyroidism but it should be borne in mind that a clarification of microscopic conditions is of great importance regarding further developments.

Moreover, x-ray therapy in the treatment of malignant tumors was a failure (Meyer and Ragins, Quick and Hunsberger). As to nonmalignant tumors, results of x-ray treatment are contradictory (Merritt and McPeak, Cutler and Owen, Jacob, King, and Bailey). The latter authors reported an apparent regression of parathyroid hyperplasia after irradiation, and on autopsy no parathyroid changes could any longer be found.

#### DIFFERENTIAL DIAGNOSIS

In view of the great variety of clinical pictures and the very frequent deviation of biochemical findings which in well-determined cases are so clear, and further in view of the abundance of osseous affections resembling the osseous type of hyperparathyroidism, the differential diagnosis offers a certain amount of difficulty.

As to the osseous affections resembling the osseous type of hyperparathyroidism, mention must be made of *osteodystrophy* and *osteofibrosis with parathyroid adenoma or hyperplasia*.

*Localized Osteodystrophy*—Different types of localized osteodystrophy: osteitis fibrosa localisata, brown tumor, juvenile osteodystrophy, osteoclast or bone cyst.

The differential diagnostic distinction or, to put it more appropriately, relationship between the osseous type of hyperparathyroidism, on the one hand and localized or not generalized osteitis fibrosa or whatever its name may be, on the other, lies in the following facts:

(1) In the generalized type that is, in Recklinghausen's disease or the osseous type of hyperparathyroidism the skeleton shows certain changes consisting in cysts and brown tumors which, histologically, are in nothing distinguished from the localized type.

(2) In certain cases of Recklinghausen's disease the localized manifestations were so pronounced, clinically, that they occupied the chief role in the disease and diverted attention from the essential disorder (Barr and Bulger, Stewart and Boere, Elmslie and co-workers [epulis], Churchill and Cope).

(3) In the opinion advanced by several authors, localized osteitis fibrosa may develop into the generalized type, this has proved incorrect part

in view of the fact that it has now been established that the two conditions arise from two completely different etiologic bases. In no case of osteitis fibrosa localisata were any signs of hyperparathyroidism noted nor was the calcium metabolism deranged (Mandl, 1926). The customary examinations and careful x-raying will prevent localized osteitis fibrosa, occurring as part of a generalized one, from being overlooked. The search in cases of this kind for a parathyroid adenoma or other parathyroid changes as it is often referred to in the literature but always with negative result (quoted from Weissenbach and Lièvre) is entirely without foundation.

(4) In cases apart from the strictly localized type of osteitis fibrosa there are those with multiple lesions scattered all over the skeleton. There are other cases in which all bones show cystic changes and eventually there are those with unilateral involvement of the entire skeleton on that side. Freund and Meffert refer to cases of this kind as nongeneralized fibrous osteodystrophy and give an account of seven out of a series of twenty-five patients with strictly localized disease, with extensive involvement (two with multiple localized lesions, two with diffuse monostotic lesions, and three with unilateral fibrous osteodystrophy). As it was seen from serum examinations and from further developments, these cases had nothing in common with the generalized type of the disease nor did they merge into it. None of the cases, moreover, offered any indication of parathyroid adenoma that would have produced hyperparathyroidism. In one of the cases of "unilateral" fibrous osteodystrophy the search for a parathyroid adenoma was also in vain.

It appears, therefore, that we are here dealing with a condition so far completely unclarified as to its nature which, by the way, had already received a similar name by Borak and Doll in 1934 in view of the fact that no parathyroid adenoma could be found (Mandl) (see Albright's syndrome).

Only Coenen (1937) mentioned the case of a 21-year-old girl with "unilateral Recklinghausen's disease" in whom a parathyroid adenoma was removed with permanent effect.

In 1926 I pointed out the difficulties with which the nomenclature meets in these cases.

*Paget's Disease*—The relationship between Recklinghausen's disease (the classical type of osseous hyperparathyroidism) and Paget's disease is rather a close one for several reasons although we must point out from the beginning that Paget's disease is no manifestation of hyperparathyroidism and has nothing in common with that condition.

If, however, this question arises again and again, if confusions are common and the relationship between the two conditions is constantly referred to, this is preponderantly due to the fact that for a long time no histologic differences were found between Recklinghausen's and Paget's disease. In both, the bone marrow shows fibrosis and in both, at least in the opinion of certain authors (Lièvre), cysts and brown tumors (Looser) are encountered, although this idea was rejected by Snapper. It is, however, according to the results of latest research (Knaggs, Freund, and Schmorl), the so-called mosaic structure that

is today generally accepted as a characteristic feature of Paget's disease of bones that distinguishes the two conditions (see Snapper, 1943, Plate XX).

Clinically, the two conditions offer an entirely different aspect. In Paget's disease the patient's general condition is good and the bone deformities which may persist for years without causing pain hold the foreground. An increase in the size of the skull is often the very first symptom. Paget's disease occurs in patients at an advanced age and has practically never been noted before the fortieth year of life. Spontaneous fractures are rare. There is a monostotic as well as a generalized variety.

The classical picture of Paget's disease is fundamentally different from that of Recklinghausen's disease. Regarding biochemical findings, in Paget's disease, in contradistinction to Recklinghausen's disease, calcium and phosphorus are normal in the serum and urine, while the phosphatase values in the serum may be found increased in both (Kay).

Although, therefore, the comprehensive studies by Schmorl, Léri, Gutman, and Kasabach render it practically impossible to confuse the two conditions, in the development of hyperparathyroidism and in its treatment, Paget's disease plays a certain role.

1 To begin with, in atypical cases of Recklinghausen's disease the bones may here and there show traces of recalcification which may in the x-ray view give rise to confusion with Paget's disease. This holds particularly true (Weissenbach and Lièvre) of those cases in which the development is a slow one without other signs of hyperparathyroidism (pagetoid type).

2. Provided there is a possibility of spontaneous healing in Recklinghausen's disease, as held by certain authors (Oestling), this process of recovery can manifest itself in the radiogram only by sclerosation, a condition that, in conjunction with the still existent deformities, may give rise to confusion with Paget's disease.

3. In my first patient operated upon for Recklinghausen's disease the recalcification of the bones appearing in the course of the first few postoperative weeks and months after successful parathyroidectomy was interpreted by Kienböck in a way that made it probable that the case had not been one of Recklinghausen's but rather one of Paget's disease. This objection which proved entirely incorrect was even then refuted by me (1934). Today it is generally known and has been verified on numerous occasions that the process of recovery taking place in the bones after parathyroidectomy has nothing in common with Paget's disease. In 1941 attention was drawn again to this point by Couch and Robertson.

4. In spite of the many objections, certain authors continue to adhere to the view that there exists a relationship between Paget's disease and the parathyroid glands. This is held, for example, by Donati and by Hellstrom, who distinguished a special type of hyperparathyroidism which "simulates or is complicated by Paget's disease." Ballin even went so far as to advocate parathyroidectomy in the treatment of Paget's disease which, in his opinion, should be attributed to an excessive parathyroid activity, probably since he found a

definite parathyroid adenoma in one of his cases. Churchill and Cope pointed out, on the strength of another case reported by Walker, Irving, and Aub (quoted after Churchill and Cope, that coincidence of the two disorders was recorded and verified by radiographic and chemical findings. In any event this is a very rare exception.

Gutman and Parsons gave a very instructive synopsis of 150 cases of hyperparathyroidism and 146 of Paget's disease with enumeration of the various symptoms.

In this connection it should be pointed out that especially Schmorl, for autopsies in 190 cases of Paget's disease reported not a single one in which there was any indication of hyperactivity of the parathyroid glands. Similarly, Snapper reported two cases, Mandl three, and Churchill and Cope one of Paget's disease in which no adenoma of the parathyroid could be found on operation. It appears, therefore, that Paget's disease belongs to the category of osteofibroses without parathyroid hyperfunction and that it is not connected with parathyroid adenoma.

*Albright's Syndrome*—Albright's syndrome consists of polycystic fibrous dysplasia with pigmentation of the skin associated with pubertas praecox in females, and similar conditions (Lichtenstein and Snapper).

In one of the first cases of this type, today generally known under the designation of Albright's syndrome and published for the first time by Albright in 1937, I had the opportunity of participating in the observation. I also performed an unsuccessful operation of this type. The case was then published by Borak and Doll in 1934. Since it is not known in the American literature an extract is given here:

The patient had had a vaginal hemorrhage when she was 10 years old which had persisted for several days and had recurred after three months. The abnormal development of the breasts and the pigmentation of the nipples was striking at that time. When she was 8 years of age there was hair on the mons pubis, and when she was 10, in the axillae. Height and weight, on the other hand, were not particularly abnormal. When she was 6 years of age, she sustained a spontaneous fracture of the left femur. A roentgenogram made on that occasion showed that the entire femur was changed. There was diffuse enlargement of the bone with thinning of the corticulis, decalcification, and a fracture in the subtrochanteric region. These fractures recurred at other places of the left thigh in 1932 and 1933. Healing was always satisfactory in simple plaster of Paris casts and left no callus. Apart from a waddling gait there were no particular functional disturbances.

Roentgenograms revealed that the entire skeleton including the spine, the ribs, and the left shoulder region contained the same changes as those noted in the left femur to a more or less extensive degree. The bones of the pelvis, moreover, showed a rather sharply outlined light patch, the size of a palm, just above the hip. Similar changes were found in the phalangeal and metacarpal bones, and in those of the left forearm and upper arm. At the occiput a bony swelling could be palpated. Qualitatively the bone changes were characterized by decalcification, bony swelling, and thinning of the corticulis in the long tubular bones while the short tubular bones and the occiput, although thickened, showed hyperostoses. The striking feature was the exclusive involvement of the left side of the body throughout a period of observation of four years.

In view of the high blood calcium (19.8 mg. per cent) and the excessive calcium elimination in the urine (42 mg. per day) a parathyroid tumor was searched for operatively (Mandl). On operation, a formation giving the impression of an enlarged parathyroid gland



was removed but was verified by histologic examination as consisting of purely thyroid tissue. The parathyroid glands themselves were normal. The operation had not, therefore, any objective effect, and four months later the patient had another spontaneous fracture of the femur while the calcium level of the blood remained permanently increased.

From the foregoing it can be seen that by 1934 I was able to ascertain that the syndrome was not connected with a parathyroid tumor. In the discussion taking place after Borak and Doll had presented the case, I pointed out that we were dealing with a separate syndrome which had nothing in common with hyperparathyroidism or Recklinghausen's disease.

In 1937, Albright, Butler, Hampton, and Smith reported upon five cases of that type to which Albright, Seoville, and Sulkowitch added another two in 1938. At that time it was clear that the syndrome, the etiology of which remains unclarified, had nothing in common with hyperparathyroidism and that any search for a parathyroid tumor or any operative manipulation on these lines is absurd.

Dockerty and co-workers (1944, 1945) gave a review of thirty-nine cases they collected from the literature with addition of six of their own observed at the Mayo Clinic. Nothing new could be said about the etiology which remains obscure (Mondor, Dueroquet, Leger, and Laurence, Braid, Rohson and Todd, Summerfeldt and Brown, Neller).

Other varieties of the disorder are referred to in publications by McCane and Bruch giving an account of cases including, in addition to the previously mentioned symptoms of fibrous osteodystrophy with pathologic pigmentation of the skin and pubertas praecox, the signs of hyperthyroidism. One of the cases, described by Sternberg and Joseph, is particularly interesting in view of the post-mortem which could be performed and during which especially the endocrine organs were very carefully studied. For our considerations it is worthy to note that no parathyroid changes were found. Possibly we were dealing with a certain variety of Albright's syndrome, because comparatively often more or less distinct manifestations of hyperthyroidism are met with in this disease (cases reported by Masser and Barnwell, Gaupp, Goldhammer).

The laboratory data, by the way, are normal in this condition, regarding calcium and phosphorus in the blood and urine, while the phosphatase may be increased.

It is, therefore, rather astonishing that in twenty of the cases reviewed by Dockerty and co-workers a search was made for parathyroid tumors, although it was always unsuccessful.

The osseous involvement is very frequently unilateral, and renal complications as they are customary in hyperparathyroidism are almost never encountered.

A similar condition was referred to by Lichtenstein in 1938 as "polyostotic fibrous dysplasia of bone," and later, in 1942, in a publication by Lichtenstein and Jaffe as "fibrous dysplasia of bone," a condition affecting one, several or many bones, the graver cases of which may present abnormal pigmentation of skin, premature sexual development, hyperthyroidism, or other extraskeletal abnormalities.

In 1942, these authors gave an account of twenty-three cases and it is pointed out that the condition is identical with that described by Goldhammer, Borak and Doll, McCune and Brueh and Albright with the only exception being that the osseous as well as the extraskeletal manifestations may vary in degree. In their opinion, approximately fifty-three different designations have been used for the same condition in the course of the years (osteitis fibrosa, osteodys-trophia fibrosa, focal, unilateral, disseminated, fibrocystic disease of the bone, a form of Recklinghausen, regional, or unilateral Recklinghausen). Lichten-stein and Jaffe in their statistics give a complete list of Albright's 90 cases:

In 15 out of 87, the disease showed monostotic involvement, while in 17 out of 87 several bones were attacked. In 12 of these 17 an entire limb was in-volved. In 29 out of 87 cases the skeletal involvement was more extensive but predominantly one-sided while in the remaining 26 very many bones were affected. In 32 out of 90 cases there was pigmentation of the skin and in this respect there was no difference between the two sexes. No more than 20 cases (out of a total of 90) showed signs of endocrine dysfunction (hyperthyroidism, premature sexual maturation, premature skeletal growth).

Eventually, Snapper (in 1943) referred to the same syndrome as lipoid granulomatosis of the bones without craniohypophyseal localization and reported several cases of this type. As to therapy, aluminum acetate treatment advo-cated by Helfet seems to have proved its value.

Cases of polycystic fibroid dysplasia have also been repeatedly described (Horwitz and Cantarow, Cherry, Mochlig and Schreiber) with varying localiza-tion. The case reported upon by Mochlig and Schreiber was of a large bone tumor of the skull with unilateral involvement of the skeleton of the extremi-ties. An interesting feature of the case (a boy 16 years of age) was, moreover, the coexisting hypopituitarism, manifested by gynecomastia, absence of beard and axillary hair, and puerile type of voice.

*Renal Osteodystrophy*—Various renal disorders may give rise, in contra-distinction to the primary renal type of hyperparathyroidism, to a so-called secondary hyperplasia of the parathyroid tissue. Reference to this form of the disease has been made before. They furnish the evidence that for certain osseous affections accompanied by a general parathyroid hyperplasia, Erdheim's original theory still holds true.

This renal osteodystrophy has been observed in children and adults alike. It is also found as an accompaniment of chronic interstitial nephritis in adults especially if there is simultaneous acidosis which is, by a number of authors, held responsible for the osseous changes (Mach and Rutishauser, Guye and Rutishauser, and others).

This condition in which the renal disturbance usually predominates some-times is characterized by osteoporosis, as a rule, however, by osteodystrophy. The parathyroid glands need not necessarily be enlarged and may be completely normal.

For the surgeon it is important to note that, in contrast to findings in hyperparathyroidism, the blood calcium is low and the blood phosphorus high (see Table IV).

*Various Other Osseous Affections*—To the category of other osseous affections belongs for example, the case published by me in 1935 (Case 6). Here the x-ray aspect and the existing hypercalcemia were suggestive of osseous hyperparathyroidism. But on operation, although the entire region was carefully explored, no adenoma could be detected. An enlarged parathyroid gland was removed. The calcium level of the serum dropped but the osseous symptoms increased in intensity. Only later was a diagnosis made of carcinosis of the skeleton. The calcium in the serum again rose to 16 mg per cent. On autopsy, a carcinoma of the prostate was found.

Another interesting case was reported by Rahm. The x-ray findings in a 20-year-old patient with generalized cyst formation were "typical" of Recklinghausen's disease. In 1932, an unsuccessful operation was performed for parathyroid adenoma but only a lobe of the thyroid gland was removed. The blood calcium was 12.5 mg per cent and dropped to 8.1 to 10.7 mg per cent after the operation while the blood phosphorus increased to 3.7 to 6.4 mg per cent. In 1938, the patient developed a tumor in the gluteal region. Later he died from pleural empyema and, on autopsy, hemangiomatosis of the skeleton was found with involvement of the soft parts.

The high phosphorus values are not exceptional, particularly since Rahm himself in 1935 described an osseous parathyroidism with a phosphorus level of 6.2 mg per cent presenting a typical parathyroid adenoma on operation.

However, if the calcium and phosphorus values are indecisive and x-ray findings are obscure, one should not undertake operation before making a biopsy of the bone at an easily accessible site. In a case described by Bretschger the diagnosis was established only in this way.

A rarer differential diagnostic problem was presented by the following case reported by Albright, Burnett, Cope, and Parson.

The patient, a boy 14 years of age, had a spontaneous fracture of the femur through solitary bone cyst (plaster cast). In the course of time he developed anorexia, vomiting, and hypercalcemia (14.6 mg per cent), while the serum phosphorus and phosphatase were normal. X-ray views showed decalcification of the immobilized part of the skeleton without involvement of other bones.

Since there was also hypercalcemia, an exploration of the parathyroids was twice attempted but neither an adenoma nor hyperplasia was found. The patient was immobilized and activity and weight-bearing were forced. After one month the serum calcium was normal, anorexia and vomiting had ceased, and the renal function was normal. The patient had, therefore, completely recovered.

Similar cases have been referred to by Howard and Cuthbertson.

The list of the different varieties might be continued ad libitum (myelomatosis and carcinosis of the skeleton have been referred to under Primary and Secondary Hyperparathyroidism).

## PARATHYROIDECTOMY

The method of choice in the treatment of primary hyperparathyroidism is parathyroidectomy.

It is obvious that if possible it should be tried, prior to operation, to clarify the localization of the parathyroid tumor. This can be done by palpation and also by x-raying.

Prior to and during the operation the decisive point is whether one is dealing with a normal or a pathologic situation. It is, further, of importance to be acquainted with the aspect of normal parathyroids and to know when the organ should be regarded as enlarged. The reduction of parathyroid substance requires technique other than the removal of one or two distinct tumors.

During the operation it is of greatest importance to ascertain whether the tissue that has been removed is actually that of the parathyroids.

Finally, the importance of forestalling postoperative tetany cannot be sufficiently stressed.

Since the adoption of the operative method devised by Churchill and Cope in diffuse hyperplasia (to be described later) the weight of the parathyroid tissue has also become important to the surgeon. According to Pappenheimer and Wilens one normal gland weighs 0.027 to 0.032 Gm. In a large-scale study by Gilmour and Martin comprising 527 cases, among which 301 were normal, the maximum weight of the normal organ was established as being 120.8 mg. in the male, 139.7 mg. in the female subject. In the "endocrino" group and in the "renal" group the weight increased to nearly three times the normal one (the entire gland being weighed). The weight of the "parenchyma" alone is not so much increased.

For the surgeon the pathologic localizations are of greatest significance. Among them the most important are (1) in the vicinity of the common carotid, (2) in the vicinity of the phrenic nerve, (3) in the anterior mediastinum, (4) in the posterior mediastinum, (5) within the thyroid tissue.

It is clear that parathyroid tumors may vary in localization in accordance with this outlined localization of the normal organ (to be discussed).

*Parathyroidectomy for Parathyroid Adenoma*—Palpation of a parathyroid tumor is only very exceptionally possible, in Snapper's opinion in no more than 5 to 10 per cent of cases. Usually, however, palpatory findings are misleading and what is palpated is often a thyroid lobe. Very exceptionally a silent tumor has been found on palpation while other signs of hyperparathyroidism were absent (Barker and Brines). Alexander, Kepler, Pemberton, and Broders were more successful. In their series of fourteen cases of parathyroid tumor, palpatory findings were positive in three (21.4 per cent). In two cases the parathyroid tumors had caused upward displacement of the thyroid, thus providing positive although misleading palpatory findings.

If palpation is negative or undecisive it can today be demanded that an exact roentgen examination precede the operation and that it be ascertained whether possibly the tumor lies in the anterior or posterior mediastinum where it may cause displacement of the trachea or esophagus. Cases in which a shadow

was found in the anterior mediastinum, a calcified tumor of that site, kinking of the esophagus, or posterior displacement of the trachea have been referred to by Bergstrand, Brown, Goldmann and Smyth, Snell (quoted by Snapper, 1943), Alexander and associates, Cope, Lahey, and Miller. Misinterpretation of such mediastinal shadows have also occurred. Thus, for example, Vilvandré referred to a parathyroid tumor as a mediastinal tumor of an ill-defined nature, and confusion with aneurysm of the innominate artery or substernal goiter were also reported (Hirsch). On the other hand, in a case reported by Anderson (quoted by Snapper) compression of the trachea on the right and of the esophagus on the left apparent in the roentgenogram could be diagnosed as due to bilateral adenoma which could be verified by operation.

In spite of these interesting findings it must be admitted, however, that in the majority of cases the localization of the tumor is not realized before operation and that usually a thorough search has to be made. The salient point of the operation is this search, and that, first of all, the normal sites are explored goes without explanation.

Up to the year 1933, I collected sixty cases of parathyroidectomy from the literature and out of fifty-five, in which the localization was mentioned the site of the tumor was normal in forty-three (see Table V).

TABLE V

LOCALIZATION	NUMBER OF CASES
Right	
Above	5
Below	12
Above and below	1
Left	
Above	1
Below	18

In six cases no special mention was made of the localization. From this tabulation a distinct preference appears of the lower parathyroids.

Twelve of the cases presented by abnormal localization, as shown in Table VI

TABLE VI

LOCALIZATION	NUMBER OF CASES	AUTHOR
Intrathyroidal	4	Gordon-Taylor and Handley, Wichmann, Lahey, and Gold
Underneath the left clavicle	1	Barr, Bulger, and Dixon
In the carotid triangle	2	Wilder, William, and Wellbroek
Sub-ternally	3	May and Lièvre, Walton, Hunter, and Mandl
Between esophagus and trachea	1	Walton and Hunter
Behind the trachea	1	Hunter

Therefore, in nearly 25 per cent of the cases the localization was an abnormal one. In the meantime the knowledge of this misplacement of parathyroid tumors has become rather general, although it may happen that the tumor is not found at all. Apart from the fact that I was unable to detect a parathyroid tumor, an experience of this kind has led a number of surgeons to far-reaching conclusions regarding the value of this operation in general

Let us compare the state of affairs in an operative respect with these statements.

It was reported by Alexander, Pemberton, Kepler, and Broders that nine among fourteen tumors were found on the right side while only five were on the left.

In one case the tumor was within the right lobe of the thyroid gland, was nodular and extended into the superior mediastinum. In the other 13 cases the tumor was outside the thyroid parenchyma . . . in 7 cases the tumor was situated at the lower pole of the corresponding thyroid lobe. In 3 of these cases the tumor projected through the superior into the posterior mediastinum. In one of the latter cases the tumor lay behind the trachea and esophagus. In 4 instances the tumor lay behind the corresponding lobe of the thyroid gland midway between the lower and upper poles, while in one case the tumor was found behind the upper poles. In another case the tumor lay in the left anterior mediastinum and could be removed only after the sternum had been split.

In four out of fourteen cases, therefore, the tumors were in the mediastinum, one time in the anterior and three times in the posterior one. All the tumors could be removed operatively.

Krausz, in 1939, reviewed five cases of hyperparathyroidism. Three of these patients were cured. In one who died, two tumors had been present of which, however, only one had been found on operation. In another the tumor lay behind the esophagus and could not be detected on operation. Among four tumors only one was found at a normal site. Krausz, therefore emphasized the difficulties of operative therapy.

The more diversified and the larger the series of patients the more important is it for the surgeon to have a wide experience. Thus, Cope reported in 1941 that at the Massachusetts General Hospital in Boston, up to the year 1941, sixty cases of hyperparathyroidism had been observed. Fifty-eight times the diagnosis was established during the operation and only twice on autopsy. There were fifty-four adenomas and in only six cases was primary hyperplasia found. Among the fifty-four adenomas, there were two tumors in four cases, and one in the remainder, so that there was a total of fifty-eight adenomas. Of these, eleven were in the anterior, five in the posterior mediastinum, and the remainder in the neck region.

Cope's number of mediastinal adenomas (sixteen out of fifty-eight) was, therefore, particularly great so that he undertook the important task of studying the reasons for the presence of the parathyroid tumors in the mediastinum (embryologic descent and displacement from the neck into the mediastinum). Walton was the first to perform an operation on such a descending parathyroid tumor.

Cope devised a special method for the detection of these tumors. He divided the operation into two stages, during the first of which the neck region, posterior mediastinum, esophagus, and trachea are explored. During the second, in case the tumor has not yet been detected by the first procedure, the sternum from the manubrium up to the level of the third interspace is split.

This method has already been used by Gordon-Taylor who succeeded in removing a parathyroid tumor from the anterior mediastinum by transsternal

approach (Gordon-Taylor and Handley). Cope found it necessary, however, to apply this method systematically in view of the great number of his mediastinal cases and the impossibility to reach the tumors from an incision at the neck which is very instructively illustrated by the sketch attached to Cope's article.

The recognition of intrathyroid tumors is fraught with considerable difficulty. Lahey operated upon three patients with this difficulty. No rules can be laid down as to how to conduct the search for these tumors. The unilateral "blind" thyroidectomy, in case the adenoma is not found, as a method of choice does not, in my opinion, offer a sufficient degree of certainty.

In the cases published by Schlesinger and Gold, Couch and Robertson and that by Bauer, intrathyroidal parathyroid adenomas were present.

*Secondary Operations.*—Although with advancing experience and increased thoroughness of the operation (see Cope) the number of secondary operations has surely decreased, they still play an important role in the history of parathyroidectomy as well as in actual fact. If after failure to detect an adenoma the operation is discontinued, if a tumor mass is removed which on microscopic examination does not prove to be a parathyroid tumor, or if, after an unsuccessful search for an adenoma, normal parathyroid tissue has been removed, in the majority of cases the patients are not improved and the surgeon sees himself confronted with the necessity of proceeding to another operation.

The classical case of Duhois, which was the first in which the presence of hyperparathyroidism was suspected and a search instituted for a parathyroid tumor, ran a very characteristic course in this respect (Hannon, Shorr, McClellan, and Duhois). During the first operation two normal parathyroid glands were extirpated while no tumor was found. The improvement the patient showed after the operation remains, as a matter of fact, inexplicable (high calcium diet). In the course of time, however, renal damage with stone formation became more and more pronounced. It was only during the seventh operation that a parathyroid tumor was detected in the anterior mediastinum. Churchill and Cope performed only subtotal resection of the tumor and transferred the rest from the mediastinum to the neck region. This ingenious idea to avoid tetany in the patient who had already lost sufficient parathyroid tissue, however, was not awarded by success. A stenosing calculus of the ureter had to be removed and the patient, who was already in a very poor condition, died twenty-six hours after the operation.

Up to the year 1936, Churchill and Cope's thirty cases included five of secondary or repeated operations. The interval between the first and second or third operation was, including the famous case of Captain Martell on whom seven operations had been performed, five to twelve months.

Failure to achieve success by the first operation is due to the fact that usually normal parathyroids, thyroid tissue, or thymus is removed. During the last operation, the successful one, the responsible parathyroid adenoma was three times in the anterior mediastinum, once retroesophageally and once behind the right thyroid lobe. Again Churchill and Cope proceeded in such a way as to avoid serious tetany where parathyroid tissue had been removed previously, by performing subtotal resection.

From the literature it appears that in primary hyperparathyroidism due to parathyroid tumor the extirpation of normal parathyroid tissue is of no avail and since the patient is not improved, a secondary operation usually must follow and eventually when the responsible parathyroid tumor is removed the likelihood that postoperative tetany may develop is all the greater. The contrary view I once held, and which has rightly been criticized by Snapper, I hope thus to have corrected.

*The Technique of Parathyroidectomy in the Presence of Multiple Tumors or Hyperplasia of the Entire Parathyroid Tissue.*—It is also to Churchill and Cope that we owe the technical directions for cases of parathyroidectomy with multiple tumors or hyperplasia of the parathyroid tissue. These authors were the first (1934) to recognize the existence of multiple tumors or diffuse hyperplasia of the parathyroid tissue. They were followed in short succession by publications on six cases of this type from the Boston school.

In the first case two, hyperplastic parathyroid glands were extirpated during the first operation, and during a second a subtotal resection was made on the third enlarged gland. The fourth parathyroid could not be discovered. After the operation this patient still showed a mild tendency to hyperparathyroidism.

In the second case (Case 16, Churchill and Cope) only two hypertrophic parathyroid glands were extirpated weighing 15.6 Gm.

In the following case actual diffuse hyperplasia of all parathyroids is described and all four of them were exposed. Three were totally removed, while on the fourth a subtotal resection was performed. The extirpated tissue weighed 3.4 Gm.

In three further cases of diffuse parathyroid hyperplasia the procedure was as follows (Case 23 of Churchill and Cope):

The patient had the typical aspect of skeletal and renal manifestations. A biopsy was made of a suspicious lesion which, on x-ray examination, showed atypical chondrosarcoma. On repeated examination the urine showed a small amount of Bence Jones protein body. However, calcium in the serum was increased and phosphorus was very low. During the operation (July 12, 1934) all four parathyroids were found hypertrophied: right inferior 8 by 6.3 mm.; left superior 3 by 1.7 by 0.8 cm.; left inferior 1.1 by 0.6 by 0.3 cm.; right superior 7 by 4 mm. The first three glands mentioned were extirpated while from the fourth a biopsy specimen was taken. The tissue removed weighed 2.47 Gm. There were no signs of tetany. After the operation calcium and phosphorus values in the serum soon returned to normal and the patient recovered rapidly.

Microscopically, the hyperplasia was of the type characterized by water-clear cells.

The procedure adopted by Churchill and Cope was similar in their two other cases. The three glands in which hyperplasia was of the highest degree were totally removed and on the fourth a subtotal excision was performed. The total weight of the tissue removed was 6.8 Gm. and 11.2 Gm., respectively.

The first patient developed a transient tetany while the second remained normal. Calcium and phosphorus values of the serum returned to normal very soon after the operation in both cases. The hyperplasia was in both types characterized by water-clear cells.

In broad outline this is the operative technique in the presence of diffuse hyperplasia. It was summed up by Churchill in 1937 in his "Principles of



Parathyroid Surgery" and by Cope in "The Surgery of Subtotal Parathyroidectomy." From practical experience it appears that the procedure advocated by Churchill and Cope is the right one.

*Tetany*—In view of the fact that tetany (hypoparathyroidism) is a very serious postoperative complication it seems worth while to discuss this point in greater detail. In the third patient I operated upon, in 1933, a very peculiar type of late tetany with mental disturbances was noted which was, no doubt, the reason why the patient died. Such "confusional states" have been referred to elsewhere (Ask-Upmark, Wanke) and are beyond any doubt connected with the existent tetany. Among fifty-five patients operated upon up to 1932, I found postoperative tetany in nine, five of the patients recovering (Hunter, Snapper, Gold, Elmslie and associates), and four dying either during or immediately after the operation (Beck, Wanke, Ask-Upmark, Mandl). It was particularly the case reported upon by Beck in 1928 that, two years after the first successful operation, contributed much to discrediting the operative method. As I was able to ascertain, in several of the cases an excessive amount of parathyroid tissue had been removed, frequently normal and abnormal tissue together.

Up to 1936, McClure reported 125 cases of hypoparathyroidism he had found in the literature in which an adenoma had been extirpated in toto or in part. At the time when he made his report, eleven patients had died after the operation, seven with signs of hypoparathyroidism, of whom three had succumbed to this complication.

The same author described a case of tetany developing after extirpation of a parathyroid adenoma because of hyperparathyroidism, which is the first case of this type published in America (Wilder, Camp, Robertson, and Adams). McClure added one of his own cases, in which the patient died, four months after parathyroidectomy, from tetany.

A renewed perusal of the literature, however, shows that neither the statement I made in 1933 nor the view held by McClure is in conformity with actual facts and that tetany certainly appears much more frequently after operation for hyperparathyroidism, although it is now possible by various measures (to be discussed) to forestall fatal tetany. Thus, for example, among the first eighteen cases reported upon by Lièvre in 1932 nearly 50 per cent of the patients developed tetanic manifestations and Braine (1935) even reported tetany in 67 per cent of all operations for hyperparathyroidism. From more recent publications it appears that it was, first of all, the Boston group that approached the study of the problem of how to avoid postoperative tetany and introduced a special operative method for this purpose ("Conservative Surgery," Churchill and Cope). It appears, therefore, that the development of postoperative tetany after operation for hyperparathyroidism is generally feared. The second group of authors taking up the study of this question on a larger scale (Mayo Clinic) have now in their latest series of observations, published figures (Keating and Cook) which are of greatest significance for the understanding of the problem. While Churchill and Cope were guided, first of all, by the wish to reduce the parathyroid tissue and made important con-

tributions to this end, Keating and Cook in their recent series of twenty-five cases of hyperparathyroidism found that in 50 per cent of cases tetany developed in all three groups. Within the three groups, the distribution was six times in the group of classic bone disease. In this category comprising seven cases, it appears that there was only one with no manifestations of tetany. It must be pointed out, however, that among these six there was only one case of a severe character. Of nine cases of the second category, minimal bone disease tetany was noted only twice, while in the third group of eight cases without evident bone disease, tetany occurred only four times. Regarding the frequency and severity of this complication, the first group is certainly leading and Albright's old theory, which had already been confirmed by Jaffe and Bodansky, implying that there exists a relationship between tetany and the degree of bone changes or the level of the alkaline phosphatase values (danger limit, 14 to 20 units), seems to find confirmation (Albright).

Another important point is whether or not there exists a difference between hypoparathyroidism with tetany after operation for goiter and the type developing after operations for hyperparathyroidism. No doubt, after an ordinary goiter operation tetany is much rarer than after operation for hyperparathyroidism.

Swiss authors (Clairmont) quoted  $1\frac{1}{2}$  per 1,000 for Bern and 4 per 1,000 for Zurich, which is similar to American figures (Crotti, six times among 7,500 operations). It appears, therefore, that with improving technique postoperative tetany no longer plays a major role. Swinton gave 0.2 per cent for 15,552 thyroid operations of the Lahey Clinic.

Conditions are different where hyperparathyroidism is concerned. Here operation consists in at least the removal of excessively functioning parathyroid tissue, and the likelihood for hypoparathyroidism to develop is, therefore, far greater than after an ordinary goiter operation.

As a rule, after operation for hyperparathyroidism the originally high blood calcium drops abruptly, frequently below the tetanic limit (7 mg. per cent). Two other factors are likely to reduce the activity of the remaining parathyroid tissue or even to abolish it altogether. First of all, we know nothing about the state of activity of the normal parathyroids remaining in the organism. Even if they are of normal size, they may be inactive after the entire activity has been taken over by the adenoma removed (Mandl). So far nothing is known about the function of this normal parathyroid tissue prior to and after the extirpation of a hyperactive adenoma. Account should be taken further of the calcium hunger of the osteoporotic skeleton after operation on a parathyroid adenoma (Snapper), likely to intensify the hypoparathyroid tendency. "After the operation the decalcified skeleton absorbs the calcium from the plasma with so much avidity that the calcium current which, before the operation, went from skeleton to blood, is reversed. The quantities of calcium which are now withdrawn from the blood plasma are so large that hypocalcemia and tetany result. Even the presence of three remaining normal parathyroids is then not sufficient to keep the calcium metabolism in its normal pathways." On the other hand, if tetany develops after an operation for

primary diffuse hyperplasia of parathyroid tissue, the explanation is rather simple: it occurs as a result of extirpation of excessive amounts of parathyroid tissue. In cases of this type the prevention of tetany is a technical question (Churchill and Cope).

A perusal of the literature concerning postoperative tetany after operation for hyperparathyroidism yields no indication of a relationship between a high preoperative calcium value in the blood and the postoperative hypoparathyroidism.

Jaffe and Bodansky pointed out that the more intense the bone changes the higher the phosphatase and the higher and the more difficult it is to control hypocalcemia following a successful parathyroidectomy, in other words, the severer postoperative tetany. The authors explain it by the depletion of the skeleton "which represents a sort of vacuum which greedily sucks in for repair considerable circulating calcium, thus tending to create a prolonged postoperative hypocalcemia."

This biochemical explanation for the theory of the calcium hunger of the skeleton does not apply to all cases. On the other hand, tetany is not necessarily always accompanied by a low calcium level in the serum. I saw cases of tetany with 11 to 12 mg. per cent of calcium and others which with a calcium level of 5 to 6 mg. per cent developed no tetany.

On the whole, it may, therefore, be said that the occurrence of postoperative tetany cannot be foretold with certainty from preoperative findings and that an adequate amount of caution during the operation is often able to prevent it. It is for this reason that Churchill and Cope (1936) suggested removing part of the adenoma only if a postoperative tetany had to be feared and moving the remainder of the adenoma superficially into the neck region so that it might be removed easily in case the operation was not completely successful. This "conservative surgery" should be adopted, according to Churchill and Cope, (a) if the phosphatase value is higher than 14 Bodansky units, (b) in the presence of sepsis and general debility, (c) in renal dysfunction since in that case tetany is more difficult to control, (d) in an "unknown status" of the normal parathyroid glands as in secondary operations, (e) in an "unknown status" of the other parathyroids when dealing with multiple adenomas.

Similar ideas were expressed by Albert at the International Congress of Surgeons in 1935.

Measures to control tetany are: (1) administration of calcium per os or intravenously, (2) administration of vitamin D, (3) administration of parathyroid extract, (4) administration of A. T. 10 (dihydrotachysterol, Hiltz, 1933), and (5) implantation of parathyroid tissue.

No detailed account can be given here of therapy. It should only be mentioned that the use of parathyroid extract is frequently followed by immunity to this treatment so that progressively increasing doses are necessary to maintain a normal calcium balance. It may even occur that intolerance to parathyroid extract develops (Anb, Wilder, Camp and Ochsner, Robertson and Adams, McClure, and Clairmont).

A considerable improvement of tetany therapy was the discovery by Holtz of A. T. 10 which is synthesized from ergostetrine. Independent of the original level it specifically increases the serum calcium. The effect does not set in before the lapse of twenty-four to forty-eight hours and constant checkup is necessary to avoid severe hypercalcemia.

A detailed report on this preparation was given by Bauer at the International Congress of Surgeons in 1935, and the indication, the shortcomings, and the danger of its use discussed. The difference between this method of treatment and that with parathormone is shown in Table VII.

TABLE VII

	PARATHORMONE	A. T. 10
Administration	Parenteral	Peroral
Effect	Immediate, rapidly subsiding	After 2 to 3 days, persistent
Dosage	1 to 2 times per day	Once a week
Serum calcium	Increasing, fluctuating	Increasing, constant
During acute attack	Immediate effect	No effect

Although A. T. 10 is of no avail during an acute attack, it is certainly very effective in chronic cases (Swinton, Brunner). Ineffectiveness of A. T. 10 has recently been reported (Stahl), a fact that was corroborated by Holtz.

There are authors who advocate, in cases of a chronic type, recourse to the old method of transplantation of parathyroid tissue (Braine and Rivoire, Mason and Warren).

#### RESULTS OF OPERATION

After the parathyroid tumor or the two tumors or, in the presence of diffuse hyperplasia, a sufficiently large amount of parathyroid tissue has been removed, the result of the operation manifests itself very rapidly. Snapper in his first case, similar to my first case, was able to ascertain an effect of the operation as soon as twenty-four hours after. Goldmann gave an account of a case in which after parathyroidectomy the preoperative calcium level of 19 mg. per cent dropped to 10.5 mg. per cent within six hours. This progressive improvement is in the subsequent few days threatened only by an intervening tetany and later by complications of the urogenital tract. The condition of the bones progressively improves during the first few months and the majority of authors report recalcification of the skeleton.

This much-discussed development of my first operation, in which the disease recurred after a complete cure of six years, gave rise to the anxious question as to whether the operation was of any permanent value at all and whether the other patients operated upon in the meantime were not threatened by a similar fate after an initial success. Today we are in a position to say that, fortunately, this fear was unfounded. Although the majority of authors still devote the greatest part of their attention to a further study of the disease and the diagnostic and technical possibilities, giving little information on the permanent results after operation, a number of data are available. Thus, for example, Snapper reported that his first patient died ten years after successful operation from coronary thrombosis, while the second was still in

a satisfactory condition after nine years (1939), and the third, operated upon in 1934, was in an excellent condition in 1940.

Coryn's patient, after four years was in so satisfactory a condition that osteotomy for the correction of deformity could be performed.

In a case reported by Wichmann the condition was still good after eight years. In several cases of Alexander, Pemberton, Kepler, and Broders the case reports published in 1944 to some extent include the results after an appreciable follow-up period. One patient (Case 1) operated upon in 1929 died in 1940 from esophageal carcinoma; the second (Case 2) operated upon in 1930 was still healthy after six years. For the other cases no follow-up data are given.

McClure and Lam, reported upon "End Results in the Treatment of Hyperparathyroidism." Five of their six patients submitted to operation. One of the patients operated upon died four months after the operation in a state of hypoparathyroidism, while the other four, whose conditions were followed very carefully for from four to eight years, are referred to by the author as normal individuals.

Himmelmann's patient was still healthy after four years and that of Laewen after two years. A patient reported upon by Rosenbach was still cured after eight years.

These data may suffice to demonstrate that the patients had fully recovered and that the operation had been of permanent value.

Although it is with great satisfaction that we may view the results of the development of hyperparathyroidism research during the past twenty years, a number of questions are still open and further studies will find a wide and fruitful field.\*

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\*The interrelationship between hyperparathyroidism and the endocrine organs could just as little be discussed as the indication for thyroidectomy in other disorders.

endocrine  
thyroides

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## Book Reviews

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**Peripheral Nerve Injuries. Principles of Diagnosis.** By Captain Webb Haymaker, M.C., A.U.S., Army Institute of Pathology, and Major Barnea Woodhall, M.C., A.U.S., Chief Neurological Section, Walter Reed General Hospital, Washington, D. C. Pp. 227, with 223 illustrations. Philadelphia, 1915, W. B. Saunders Company.

This little book is most valuable because of the manner in which it presents material rather than because it contains new information.

Many simple line drawings and good photography simplify the anatomy of nerve injuries and the tests for loss of nerve function. A very admirable feature is the sensory deficit depicted on the photograph or on a line drawing which accompanies the photograph. One not familiar with the anatomic detail of nerve injuries will find it possible to comprehend the anatomy of these injuries with a minimum of effort through the use of this book.

It should be a very useful volume for every practitioner who has occasion to examine for, or treat, nerve injury.

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**Anesthesia in General Practice.** By Stuart C. Cullen, M.D., Head of Division of Anesthesiology, Department of Surgery, State University of Iowa Hospitals; Associate Professor of Surgery (Anesthesiology), State University of Iowa College of Medicine. With a Foreword by Frank R. Peterson, M.D., Professor and Head of the Department of Surgery, State University of Iowa College of Medicine. Pp. 260, with illustrations. Chicago, 1916. The Year Book Publishers, Inc. \$3.50.

It is always a pleasure to read a book of this caliber. Dr. Cullen has the skill and ability to write both authoritatively and clearly as well as concisely. This book contains material which should recommend it not only to students of anesthesiology but to others as well. The chapter on preanesthetic medication might well be used as a basis for interns, and surgeons, too, who are called upon to order for patients preoperatively in hospitals where this duty is not taken care of by the department of anesthesiology. The chapter dealing with ways and means of maintaining an adequate airway in unconscious patients might very well be made required reading for all personnel who have entrusted to them the care and responsibility of the unconscious patient. This, of course, includes nurses.

The book is small and easily carried. The paper is good and the printing excellent. It is well bound. It is recommended without any reservations.

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**The Peripheral Circulation in Health and Disease. A Study in Clinical Science.** By Robert L. Richards, M.D., with a foreword by J. R. Learmonth, O.B.E., Ch.M., F.R.C.S.E. Pp. 153, with 104 illustrations. Edinburgh, 1916, E. & S. Livingstone.

This 153 page monograph on the peripheral circulation covers in an admirable way the fundamental physiology of regulation of vascular tone in health and its pathologic variations in the common types of arterial disease in the extremities. Of particular interest are the discussions of nervous and local control of the peripheral vessels in Raynaud's disease, other conditions which give rise to the Raynaud phenomenon, and the description of circulatory abnormalities which are found after complete or partial injuries of the peripheral nerves. There is also a valuable chapter on the circulatory disturbances encountered after exposure to cold, particularly the wartime syndrome of immersion foot, which was studied so carefully by the Edinburgh school.



# SURGERY

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## Original Communications

### THE SURGICAL TREATMENT OF ANEURYSMS OF THE ABDOMINAL AORTA

GEZA DE TAKATS, M.D., AND JOHN T. REYNOLDS, M.D., CHICAGO, ILL.

(From the Department of Surgery, University of Illinois College of Medicine, the Research and Educational Hospitals, and St. Luke's Hospital.)

WHILE the aneurysms of the abdominal aorta are less frequent (a ratio of 1.7 to 1:10) than those of the thoracic,<sup>1</sup> more than 500 cases have been reported in the literature. Of these, thirty patients have had surgical treatment, the first case being that of Cooper who in 1817 first ligated the abdominal aorta for a left iliofemoral aneurysm with a survival period of three days.<sup>2</sup> During a symposium of the American Surgical Association on aneurysms and vascular surgery, both Bigger<sup>3</sup> and Ilkin<sup>4</sup> gave a complete tabulation of all operated cases up to 1940. Matas<sup>5</sup> from his vast experience with aneurysms at all locations reported seven cases, one of which was ligated, three wired, and three simply explored. He also published in detail<sup>6</sup> a report of the successful ligation of a syphilitic abdominal aneurysm in a patient who lived seventeen months and died of pulmonary tuberculosis with a well-obliterated aneurysmal sac and good collateral circulation.

The number of patients who have survived the surgical treatment of these aneurysms by more than one year is only six (Table I). Of these six, cotton tape has been used in five, and fascia lata in one, this is Bigger's successful case in which a second operation was done and an aneurysmorrhaphy was performed. Since this symposium the significant case report of Morton and Scott<sup>7</sup> appeared. In their patient a slowly leaking abdominal aneurysm was treated by two tape ligatures below the origin of the inferior mesenteric artery. A large left retroperitoneal hematoma was found and this may have well interfered with the collateral circulation in the left lower extremity, which subsequently became gangrenous and required amputation at a high level in the thigh. The patient died seven months after ligation of the aorta. A new aneurysm had formed proximal to the ligature which ruptured into the small intestine. The circulation of the right lower extremity was quite satisfactory, the right iliac

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outer tube of clotted blood compressed the inner tube of these arteries, thus producing occlusion. In the region of the rent of the aorta, 3.5 cm. above the aortic valve, atheromas were noted, the outer tube had ruptured into the pericardium which contained at least 300 c.c. of clotted blood.

The second patient was middle-aged, normotensive, nonsyphilitic and had a palpable aneurysm of the abdominal aorta; in addition, one popliteal artery showed a marked saccular aneurysm, whereas the other popliteal artery suddenly became occluded following trauma during a fishing trip. While no mass could be palpated it was thought likely that this occlusion represented an acute traumatic thrombosis of a popliteal aneurysm, which is not infrequently bilateral. The origin of these multiple aneurysms is unclear although a mycotic lesion was suspected by the internist. Exploration had been refused. The patient underwent a cordotomy for the foot pain and the abdominal mass steadily enlarged. The patient suddenly died in February, 1946, twenty-two months after the onset of symptoms.

The remaining six patients\* were operated upon and their case histories in abstract briefly follow.

#### CASE REPORTS

**CASE 1** (No 49072 St Luke's Hospital) — 8 K, a 69 year old farmer, entered the hospital on Oct 11, 1943, complaining of dizzy spells and a drawing, aching sensation in the abdomen, radiating to the small of the back and into both hips. He noticed a pulsating mass in the lower part of the abdomen.

Past history revealed that since February, 1941, the patient had had repeated attacks of dizzy spells which were relieved by recumbency. At that time he was told of his high blood pressure. Upon arising he felt a tightness in the abdomen and in placing his hand on it he discovered its pulsation. He vomited a few times after the dizzy spells. There was occasional blood in the stool.

On entrance there was a hard pulsating mass 5 cm. long and 3 cm. wide just to the left of the umbilicus. The mass was freely movable, not very tender, and showed a systolic expansion and bruit. Both iliac arteries seemed rather large, particularly the left, so that a second aneurysm here was suspected. The pulsations and oscillometric curves at both ankles were decreased.

On x ray the thoracic aorta showed no unusual enlargement or calcification. In a lateral roentgenogram of the abdomen a dense deposit of calcium was seen in the wall of the aorta and also in the iliacs. The fourth lumbar vertebra showed some evidence of compression. The blood Wassermann reaction was negative. Blood pressure was 150/90 mm. of mercury which rose to 190/110 mm. of mercury after bilateral iliac compression.

Operation was performed on Oct 16, 1943, with a diagnosis of abdominal aneurysm of the aorta (G. de T.). The entire abdominal aorta was enlarged, but just below the origin of the inferior mesenteric artery a fusiform aneurysm was encountered extending to the iliac bifurcation. It was the size of a large grapefruit. After the peritoneum was split and the duodenum mobilized, the aorta was encircled above the aneurysm with an inch wide eight-ply layer of cellophane which was sutured snugly with cotton around the aorta. The operation was done under pantocain-glucose spinal anesthesia. The surgical convalescence was uneventful.

During the postoperative course the patient was reexamined monthly. Eight months after operation the size was decidedly smaller. He refused a second operation for complete

\*One additional patient has been operated on in the Vascular Surgical Unit at the Veterans Hospital, Illinois, by Dr. O. C. Julian. The aneurysm shrank markedly and was palpable only on deep pressure.

ligature over the cellophane band; thirteen months after operation the mass was one-third of its previous size. He again refused operation and returned to Pennsylvania. He died suddenly on December 13, fourteen months after operation, from internal hemorrhage.

The relief from pain and the shrinking of the pulsating mass were striking. Since the iliac arteries were patent and since a partial occlusion of the aorta had undoubtedly been accomplished, an occluding ligature was suggested, but refused. The patient was 70 years old by this time and showed generalized arterio-sclerosis. He survived the banding with cellophane for fourteen months.

CASE 2 (No. 57253 St. Luke's Hospital)—W. T., a 55-year-old railroad executive, entered the hospital complaining of severe abdominal pain radiating to the small of the back, of one year's duration.

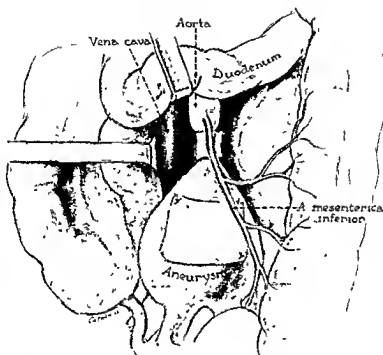


Fig. 1 (Case 2)—Aneurysm of the abdominal aorta. The sac extended from the origin of the inferior mesenteric artery to the iliac bifurcation but it was possible to separate the inferior mesenteric artery from the sac and place an inch-wide eight-ply strip of cellophane around the aorta. Over a large, necrotic atheromatous plaque a sheet of eight-ply cellophane was sutured on Dec. 4, 1944.

Past history revealed that he had known of the high blood pressure for several years and was under expert medical care. Three months prior to entrance he was hospitalized and a pulsating abdominal mass discovered. Since that time he had attacks of severe girdle pain which lasted from hours to days. He noticed that the mass was getting larger.

At the time of entrance, blood pressure was 204/110 mm. of mercury. He was slightly deaf and had a parkinsonian tremor. The heart was enlarged to the left with a loud systolic murmur at the apex. There was a visibly pulsating mass in the abdomen to the left of the

umbilicus. The chest roentgenogram revealed a diffuse dilatation of the thoracic aorta. The Wassermann reaction was negative. Stools were negative for blood.

Operation was performed on Dec. 4, 1914, under spinal anesthesia with pantocain-glucose (G. de T). A saccular aneurysm of the abdominal aorta was found extending from just below the inferior mesenteric artery to the bifurcation of the iliacs. On the summit of this sac was a greenish, partly necrotic aortic plaque which rose with each pulsation and whose extrusion seemed imminent. Wiring of this sac did not seem justifiable. An eight ply layer of cellophane was wrapped around the aorta proximal to the sac and also around the anterior surface of the sac (Fig. 1). The sac could not be encircled posteriorly, since it was firmly fixed to the spinal column. The cellophane was covered with the coat of the mesentery and the omentum. The loops of small bowel which were adherent to the sac were disturbed as little as possible. The patient's pressure fell twice during the operation but could be readily restored with neosynephrin.

During the postoperative course the thiocyanate level was maintained at therapeutic levels. Three months after operation the blood pressure was 210/130 mm. of mercury. The mass was one third of its previous size. All abdominal pain had disappeared. The patient returned to work. At nine months the mass was quite hard, still receding. It seemed close to the abdominal wall. There were no symptoms. Blood pressure was 210/140 mm. of mercury. At fourteen months there were no symptoms and he was working a full day. The cellophane created a hard, turret shaped mass over the threatening perforation and could be well palpated through the abdomen.\*

CASE 3 (No. 307205 Research and Educational Hospital)—W. McC., a 57 year old white man, was well until six months before entrance, at which time he noticed a moderately severe pain in the left lumbar region which was severe enough to disable him for four days and require a hypodermic for sedation. The pain was constant and aching in character. The following four months the patient had no complaints. Two months prior to admission the patient had a recurrence of severe aching pain which sometimes appeared to be referred to the left groin and testicle. For relief from this pain the patient went to Cook County Hospital and here x-ray views revealed the presence of a mass outside the bowel in the abdomen which was consistent with an intra-abdominal or retroperitoneal mass, the pyelograms were normal and fluoroscopy of the abdomen showed some calcified plaques about the tumor mass but no erosion of the anterior vertebral bodies. In the two months before admission the patient had noted presence of this mass in the left side of the abdomen and had noted that it pulsed but he had not noted any marked change in the size of the mass. During these two months the patient had had some weight loss which he attributed to anorexia during the periods when the pain was severe. He had also been suffering from some orthopnea and had dyspnea on mild exertion lately.

On entrance, physical examination revealed mild orthopnea, a blood pressure of 130/100 mm. of mercury, a heart enlarged to the left, a pulse rate of 76, a thrill over the precordial area, a rasping thrill over the aortic arch, and a loud systolic murmur over the aortic ring. In the left side of the abdomen opposite the umbilicus was a mass about the size of a grapefruit which was hard but compressible and which was slightly tender to palpation. The mass though pulsating was hard to call definitely expansile. An electrocardiogram showed left axis deviation, ventricular extrasystoles, and signs of left ventricular hypertrophy. Spinal Wassermann was normal. Examination of the chest showed generalized increased bronchovascular markings, moderate enlargement of the left ventricle with diffuse dilatation, and tortuosity of the aorta. The lower third of the esophagus was displaced anteriorly and to the right by diffuse enlargement of the thoracic aorta. Intravenous pyelograms showed a moderate degree of lateral displacement of the left ureter which might be due to pressure from an abdominal aneurysm. An irregular calcified mass was also noted in the abdomen overlying the left psoas muscle which was not of definitely determined origin.

\*Two years after operation the patient died with a growing mass in the upper part of the abdomen. Autopsy was not permitted.



On July 5, 1945, because of the age of the patient and the feeling that gradual stenosis of the aorta was the only safe way to handle what was felt to be an aneurysm of the abdominal aorta, under spinal and supplementary anesthesia the aorta was dissected free by opening the lesser peritoneal cavity, reflecting the pancreas upward, and separating the left renal vein from the aorta (J. T. R.). Dissecting between the vena cava and the aorta, the aorta was encircled by four thicknesses of three quarter inch wide cellophane twice proximal to the aneurysmal dilatation. It was the impression that this was done distal to the renal vessels though these were not dissected out, since it was felt that the small occlusion that would ensue would promote development of collateral circulation through the branches of the celiac if necessary. The postoperative course of the patient was uneventful except for some pain immediately following surgery.

The patient was contacted by telephone on Aug 23, 1945, at which time he had no more pain in the abdominal mass but a great deal of pain in the small of the back which



Fig 2 (Case 3)—Aneurysm of the abdominal aorta, specimen obtained at autopsy. Note the widened aorta with calcified plaques with a sudden increase in diameter. The cellophane band is partly visible at the level of the small wooden peg. There is a narrow central lumen, lined with a partially organized mural thrombus which in turn is surrounded by a thick, calcified, partly atheromatous wall. The lesion extended to the iliac bifurcation which is beyond the bottom of the picture.

did not appear to be quite explicable. The mass in the abdomen had not increased any in size and the original pain associated with the development of the mass was not present.

He was re-admitted to Research and Educational Hospitals on Feb. 5, 1946, because of a steadily increasing pain and loss of weight. He was steadily going downhill. He had started vomiting blood at intervals and had tarry stools. The respiratory distress increased and he expired on March 14, 1946, approximately one year after the onset of symptoms.

Autopsy (A 44 of 1946) revealed a greatly enlarged heart with a complete occlusion of the left descending branch of the coronary artery. The thoracic and abdominal aorta contained many calcified plaques. The abdominal aorta from the diaphragm to the iliac bifurcation was greatly dilated measuring 9 cm in external diameter. Approximately 13 cm above the bifurcation of the aorta a cellophane band surrounded the aorta. Anteriorly this 1.5 cm. wide band was imbedded in fibrous tissue, but posteriorly it lay free between the aorta and the vertebral column. There were large intramural pockets of atheromatous material and the calcified inner layers were brittle. The lumen of the aorta was partially occluded by a thick laminated layer of organized blood, leaving a central tube approximately the width of a normal aorta. The renal arteries were patent, the superior mesenteric artery and the celiac axis were demonstrable, but the inferior mesenteric artery could not be located (Fig. 2).

There was a shallow transverse erosion of the second lumbar vertebra, explaining the high root pain. The aorta did not appear constricted at the region of the cellophane band. The tissues around the band, however, were markedly fibrocell and infiltrated by inflammatory cells. A sinus tract extended from the cellophane band into a blind pocket of dense fibrous tissue. This was lined with granulation tissue showing marked inflammation. Macrophages containing black and yellow material were numerous in the sections.

Death was ascribed to myocardial failure due to coronary insufficiency and complicated by bronchopneumonia. Chronic passive hyperemia was found in the lungs and liver.

*Comment*—This patient certainly seemed past the stage of operability; both the thoracic and aorta were involved. The rigidity of the dilated aorta and the extent of the lesion made this therapeutic attempt rather hopeless. It is interesting that the occlusion of the inferior mesenteric artery, which no doubt was gradual, could be tolerated.<sup>11</sup> The findings at autopsy showed that the patient had cured the aneurysm by thrombotic occlusion and central canalization but the adjuvant role of the cellophane in this process must be considered as highly doubtful. While fibrosis was produced, this could hardly have been sufficient to produce partial occlusion of the aorta.

**CASE 4**—M. H., a 54 year old colored laborer, was well until July, 1943, when "lightning like chest pains" encircling the lower end of the chest appeared. In December, 1943, with a diagnosis of syphilitic aneurysm of the abdominal aorta, the sac was wired through a laparotomy at Cook County Hospital (J. T. R.). The patient improved for six months after which recurrence of pain led to a second wiring through the left lumbar region into which the pulsating mass had protruded in July, 1944. This again led to some relief, but in November, 1945, because of intractable root pain, a high colostomy was performed at the Neurological Institute of the University. He died in the next twenty four hours. Autopsy could not be obtained.

**CASE 5** (No. 263645 Research and Educational Hospital)—R. B., a 52 year old white man, was admitted on Feb. 6, 1941, complaining of a swollen, ulcerated left leg for the past ten years, swelling in the left groin of three years' duration.

Past history revealed that in 1926 he had injured the left ankle, eventually resulting in an ulcer of the left leg which had remained for the past ten years. He first received local treatment but in 1933 the ulcer was diagnosed as syphilitic. The patient was told he had syphilis. About two years before, he had noticed a mass present in the left lower quadrant with associated pain.

On entrance, physical examination revealed a well-developed, well-nourished Mexican man, 52 years old, lying comfortably in bed. Heart rate was 61, rhythm regular;  $\frac{1}{2}$  inch enlargement of the heart to the left. A soft, systolic murmur was heard in the apex. Blood pressure was 115/70. The lungs were negative. A mass was found in the left lower quadrant of the abdomen directly above the symphysis and extending bilaterally to both inguinal regions, both masses pulsated with the heartbeat; heart was present over the mass. The left leg was enlarged, the thigh was indurated; a large ulcerated area was present in the lower left leg. Edema of the left foot was also present. Compression of the mass above Poupart's ligament caused a bradycardia, slowing of rate from 76 to 60, therefore it was thought that the communication was between the region of the femoral and iliac junction. Spinal fluid was clear, urine negative, red count on admission was 44; white count, 41; hemoglobin, 10. Serology was positive, blood chemistry essentially normal at all times.

Exploratory laparotomy was done on Feb. 19, 1941 (G de T). Left rectus incision was made below the umbilicus. A large retroperitoneal grapefruit-sized pulsating mass presented itself when the peritoneal cavity was opened. The common iliac artery was extremely dilated and a large aneurysmal sac was present, this sac also involved a portion of the terminal aorta. The exact extent of this involvement could not be determined, therefore no ligation was attempted. The inferior mesenteric artery was involved in the mass. It was felt that the lesion was inoperable and closure was made in layers.

The postoperative course was seemingly uneventful with good healing of the wound until the thirteenth postoperative day, at which time the patient suddenly expired due to the rupture of the aneurysm.

This diagnosis was subsequently verified by autopsy, the diagnosis being rupture of varix of left external and internal iliac veins on the basis of an arteriovenous aneurysm; hemiparalytic, syphilitic aortitis. Fusiform aneurysm of the aorta, fusiform aneurysm of the left common internal and external iliac arteries.

*Comment*—This was an unusual case, since the syphilitic abdominal aneurysm of the aorta must have eroded first into the left common iliac vein. An arteriovenous fistula on a syphilitic basis has not been found in the literature available to us. The case was obviously inoperable.

CASE 4—A 54-year-old colored laborer, entered the Research and Educational Hospitals as an emergency case on Sept. 27, 1945.

Past history revealed that he had had pain in the epigastrium since 1941. A hard, pulsating mass was discovered high in the abdomen in the same year. He was known to have had syphilis and had had adequate treatment.

On entrance to the hospital the patient was in excruciating pain. He was cold and clammy and blood pressure was 80/50 mm. of mercury. There was a huge pulsating mass filling the entire abdomen. The left lower extremity was cold, pulseless and greatly swollen. It was felt that the aneurysm was leaking around the iliac bifurcation, occluding both the iliac artery and vein. The nonprotein nitrogen was 39 mg. per cent.

The patient slowly improved on bed rest and parenteral feeding. The swelling improved somewhat and the femoral arterial pulsation reappeared but no pulsations were present in the popliteal arteries. The foot remained in a precarious position. On Oct. 9, 1945, two weeks after entrance, exploration was done under spinal anesthesia (G de T). The aneurysm extended from the celiac axis to the iliac bifurcation and occluded the left common iliac vein. The left common iliac artery was patent but there was considerable mural thrombosis in the main sac which must have thrown a shower into the left lower extremity. The abdomen was closed since the case was judged inoperable.

Follow-up study showed that there was progressive canal obstruction. Both legs began to swell and the scrotum became edematous. A telephone call received two months later revealed that the patient was repeatedly tapped for ascites indicating obstruction in the portal system. He died at home.



plete occlusion taking nineteen months. They suggested the use of this substance for gradual occlusion in aneurysms of the aorta. That gradual closure of the aorta, especially at its lower end just above the iliac bifurcation, is tolerated is best exemplified by a goodly number of patients whom we have seen with saddle thrombosis developing slowly at the site of atheromatous plaques. While such patients have emaciation and complain of loss of penile erection and ejaculation, the viability of the limbs is maintained. In doing lumbar sympathectomies for such a group, the size of the lumbar arteries, serving as

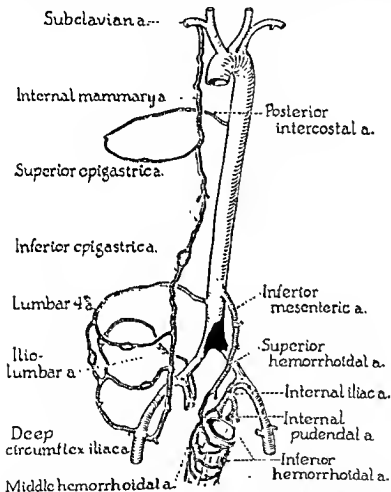


FIG. 3.—Diagram of collateral circulation in slow occlusion (gradual saddle thrombus) of the aorta. The first pathway through the internal mammary is active only in high aortic occlusions as in coarctation of the aorta but in low occlusions may play only a secondary role. The anastomosis of the branches of the superior hemorrhoidal with the middle and inferior hemorrhoidal vessels, and from them to the internal iliac artery may be palpated occasionally as pulsating vessels through the rectal wall. The most important vessels are the intervertebral (intercostal and lumbar) arteries, of which only one is shown, as they connect through the ilio-lumbar to the internal iliac and through the deep circumflex to the external iliac arteries. The integrity of these pathways depends the viability of the limb: a large sac or a dissecting hematoma may interfere seriously with this network. Placing a partially constricting band just below a pair of lumbar arteries stimulates their enlargement.

collaterals, is very obvious. In the accompanying diagram (Fig 3) we show the available channels, all of which require the integrity of the external iliac and the lower part of the internal iliac artery. In the injection specimen of Morton and Scott,<sup>7</sup> obtained at autopsy, one can see the great importance of the patency of the iliac arteries. Whether the lumbar arteries function or not will depend, of course, upon how many of them are involved in the intrasacular thrombus.

The use of cotton tape, which has been the most successful material for producing partial occlusion, still suffers from one defect common to all methods producing occlusion from the outside—namely, that partial or complete occlusion of a large artery by compression always leads to the death of the vessel wall.<sup>10</sup> The multiple, rubber band occlusion of Owings and Hewitt<sup>11</sup> has been put to a clinical test by Monahan<sup>12</sup> who ligated the abdominal aorta proximal to a syphilitic aneurysm in three stages—he was able to obliterate the sac, but five months after the first ligature the aorta perforated just proximal to the highest rubber band into the third portion of the duodenum. The patient also seemed to have persistent pain and eddiness in the right leg after the second ligature.

It has become increasingly obvious to us that in the presence of these degenerative lesions of the aorta, especially in the presence of hypertension, a complete ligature in continuity will not be tolerated for any length of time. Three remain other possibilities—either the production of slow fibrosis with consecutive application of collophane, followed later by wiring, the complete excision of the sac with transection of the aorta—a heroic procedure, but safer from the standpoint of proximal rupture than the occlusion in continuity, and finally a combination of proximal banding with a partial wrap of cellophane around the sac—a procedure which is simple and has been carried out in Case 2. In this one case no intestinal obstruction has been encountered after a follow-up of fourteen months. The cellophane must be guarded jealously from contact with the free peritoneal cavity. However, this risk is small if a good fibrous wall can be built up around the weak portion of the aneurysm. There is also a good possibility that the inflammatory reaction produced in the vessel wall will reach the intima and favor mural thrombosis, which is a self-healing process in aneurysmal sacs, as seen in Case 3.

#### SUMMARY

A group of eight aneurysms of the abdominal aorta have been observed. Of these, two were not operated on, two were simply explored, one was wired, and three were banded with cellophane. Of this group only the three treated with cellophane wrap survived for any length of time. One patient lived fourteen months, another died after eight months, and the third, whose sac had also been wrapped in addition to a proximal cellophane collar, is doing well at this writing.

#### APPENDUM

Since this article went to press, it became obvious that the type of cellophane used may be the deciding factor in the production of adequate fibrosis. For this reason in a recent case, not included in this series, strips of cellophane were implanted into subcutaneous pockets to study the reaction of the connective tissue of the patient, whose aneurysm was to be wrapped in cellophane.



## RESECTION OF PRIMARY LIVER TUMORS

J. W. DUCKETT, M.D., AND HENRY G. MONTGOMERY, M.D., DALLAS, TEXAS

(From the Dallas Medical and Surgical Clinic, The Baylor University Hospital and the Texas Children's Center)

**S**URGICAL removal of large masses of liver tissue has always presented a formidable problem. The chief concerns of the surgeon have been, first, the question of how much liver could be removed without seriously disturbing the function of that organ, and second, the necessity for adequate control of hemorrhage.

Recent advances in knowledge of the physiology of the liver, and gradual accumulation of clinical data from reports of surgical cases, have fairly well eliminated the fear of producing liver insufficiency by removal of large portions. Fishback<sup>1,2</sup> and others have shown experimentally that four-fifths of the liver of animals may be safely removed. The remarkable regenerative capacity of the liver partially destroyed by disease processes, as in cirrhosis, is well known. Important clinical observations include such studies as those by Turner,<sup>3</sup> in 1923, who found liver function normal after removal of an adenoma weighing two pounds, three ounces, and by Pickrell and Clay,<sup>4</sup> who removed the entire left lobe in three patients, subsequently finding liver function normal in two, and only slight retention of bromsulfalein in the third.

Of probable significance in the regenerative capacity of the liver is the rich arterial blood supply to all parts. The right and left branches of the hepatic artery anastomose freely so that if either main branch is divided during the course of a resection, the intact branch can adequately supply the remaining portions of the liver (Martens'). Although the vascularity of the liver is in one sense unfortunate from the surgical viewpoint, it is at the same time favorable to the removal of any particular part of the liver without jeopardizing nutrition of the remainder. However, extreme care must be taken to avoid damage to the main hepatic artery. Even temporary compression of the hepatic artery produces symptoms of shock, and this method of control of hemorrhage from the liver substance is consequently unsuitable. After radical operations for advanced carcinoma of the extrahepatic bile ducts, Brunschwig and Bigelow<sup>5</sup> reported autopsy findings, including extensive liver infarcts resulting from damage to the hepatic artery.

Control of hemorrhage is still the primary difficulty in liver surgery. Many methods have been used with varying degrees of success. Early resections, as reported by von Eiselberg<sup>7</sup> in 1893, and von Rosenthal<sup>8</sup> in 1897, were done with the cautery to aid hemostasis, and the cut surfaces were packed with gauze, which was later removed. In 1899, Keen<sup>9</sup> resected the left lobe of the liver for carcinoma, burning through the pedicle with a cautery, ligating the larger vessels, and closing the open part with catgut sutures and a gauze pack. Keen



reviewed seventy-six previously reported cases of resection of liver tumors. Shumacher,<sup>10</sup> in 1942, removed an angioma of the left lobe using Kelly clamps, cautery, and sutures. He reviewed fifty-six resections for angioma of the liver. Pickrell and Clay, in 1944, reported three cases of resection of the left lobe of the liver. Otherwise, only single cases have been reported.

The method for controlling hemorrhage described by Pickrell and Clay has been used by us satisfactorily in operations on three patients with liver tumors. The essential feature of this technique is the use of a line of interlocking mattress sutures passing through the liver substance proximal to the line of incision in the liver. These are placed prior to the incising of the liver, for the purpose of immediate control of bleeding by compression. In all three, the tumors were hepatomas, liver cell tumors of low grade malignancy. The first patient, a man of 73 years who is alive and well after twenty-two months, had a resection of the entire left lobe, as in all three cases reported by Pickrell and Clay. As these authors indicated, resection of the left lobe proved to be easier technically than resections of portions of the right lobe. In our second case, a child 3 years of age, a huge tumor of the left lobe invading the right lobe, was successfully resected, but the patient died six months later with recurrence of the tumor. Packard and Stevenson<sup>11</sup> reported an almost identical one. Our third patient, a child 20 months of age, had a much smaller tumor of the right lobe, and had a much more favorable prognosis.

#### CASE REPORTS

**CASE 1.**—L. K. K., a white man aged 73 years, was admitted to Baylor University Hospital, May 27, 1941, complaining of occasional nausea and vomiting with severe pain in the left upper abdomen of four months' duration, frequent belching after meals, and nocturia, one or two times, for several years.

**Present Illness.**—The onset was sudden some time in January, 1941. The patient became nauseated and vomited following the eating of fresh tomatoes. He thought he had "ptomaine poisoning." At the same time he had a cramping in the epigastrium and noted "rolling movements" and "rumbling" in the abdomen. On feeling the abdomen, the patient noted for the first time a hard lump in the upper abdomen. This mass grew slowly after he first noticed it, and on admission was about twice its original size. No other pain or tenderness was noticed except that occasionally, at frequent intervals (one or two days), a sharp pain beginning in the area of the mass radiated into the left side of the chest and neck. The patient stated that he could move the mass freely. The indigestion continued, and he belched frequently. Bowels moved regularly; there were no chylid stools or tarry stools, and no jaundice.

**Past History.**—Questioning showed the cardiovascular system negative, and the respiratory system negative, except for pneumonia seven times during his life, without recurrence in the past fifteen years. There was no additional history of chest pain. Gastrointestinal system was negative, until the present illness. In the genitourinary system, there was nocturia one to two times; no day frequency, burning, or urgency. Extremities were negative. He had fracture of the left elbow eighteen years before.

The patient led the active outdoor life of a farmer. Fifty years before, he had been bitten by a tarantula on the left cheek. This was followed by marked swelling of the face, which was treated by multiple incisions. Since that time, he had paralysis of the lower left side of the face.

**Family History.**—The patient did not remember about grandparents, but both mother and father died of "heart disease." Two brothers and a sister were living.

**Physical Examination**—Examination revealed a well nourished, well developed elderly man, with Bell's Palsy of the left side of the face, lying quietly in bed, not acutely ill. Pulse was 90; respiration, 20; temperature, 98.6° F. The head showed paralysis of muscles of the left side of the face below the forehead. Pupils reacted to light and accommodation, but he was unable to close the left eyelids; the left conjunctiva was red and inflamed. Ears and nose were negative. The neck had no masses, no Virchow's node, no visible venous pulsations. The thyroid was not enlarged. The chest had equal expansion. There was no interspace retraction or disturbance of vocal or tactile fremitus. Breath sounds were undisturbed, there were no râles, and percussion was not abnormal. By percussion of the heart the border was found 7 cm. to the left of the mid-sternal line, there were no murmurs or arrhythmia. Blood pressure was 150/75. In the abdomen there was a large visible and palpable mass in the left upper part, measuring 5½ by 7½ cm. on the surface. This mass was hard and freely movable, moving with respiration, it was not attached to the costal margin or the skin, but appeared to be attached to the liver. There was no tenderness or tympany, no other masses or scars. Extremities were negative. There were no lymph nodes in the axillae or inguinal areas. Reflexes were physiologic.

**Laboratory Studies**—Urinalyses on May 30, 1944, were negative except for 20 mg. albumin and a few white blood cells. June 3, 1944, they were essentially normal and also on June 13, 1944. Blood chemistry was as follows: May 31, 1944, urea, 19.3, urea nitrogen, 9.0; sugar, 95 mg. per 100 c.c. of blood, chlorides, 420, plasma proteins, 5.8. June 8, 1944, plasma proteins, 4.5, albumin, 2.5, globulin, 2.0. June 13, 1944, plasma proteins, 4.8; albumin, 2.5, globulin, 2.35. Blood counts were as follows: May 20, 1944, red blood cells, 5,600,000, hemoglobin, 16.4, white blood cells, 9,623, polymorphonuclears, 66 (bands, 8, segmental, 58), lymphocytes, 32, monocytes, 1, eosinophiles, 1. June 8, 1944, red blood cells, 5,200,000; hemoglobin, 15.8, white blood cells, 8,500 polymorphonuclears, 67 (bands, 5, segmental, 62), lymphocytes, 32, monocytes, 0, eosinophiles, 1.

The patient was operated upon June 2, 1944, under gas oxygen ether anesthesia.

**Preoperative Diagnosis**—Diagnosis was abdominal tumor, probably hemstoma.

**Operation**—A left hemihepatectomy was performed.

**Findings**—The tumor palpable in the upper abdomen proved to be the enormously enlarged left lobe of the liver. Beneath the serosa, tumor tissue could be seen over the entire visible surface of the left lobe. The right lobe of the liver was somewhat smaller than normal and about one half the size of the enlarged left lobe. It was essentially normal in appearance and no nodules could be palpated in its substance. The stomach was adherent to the enlarged liver along almost its entire greater curvature. There were also omental adhesions to the inferior surface of the liver. The spleen was not enlarged. The gall bladder was normal in appearance, except for some thickening and fatty infiltration.

**Technique**—A left transverse incision was made beginning in the midline, midway between the xiphoid and umbilicus, and extending well into the left flank. This was later enlarged by right angle extension in the midline to the left of the xiphoid, and the fused cartilages of the sixth and seventh ribs were sectioned. This incision allowed quite satisfactory exposure of the upper surface of the enlarged left lobe. The suspensory ligaments of the lobe were sectioned between clamps and ligated. In preparation for cutting across the isthmus between the right lobe and the left lobe, which was about six inches wide, an enterostomy clamp with rubber-covered blades was applied to the right of the contemplated incision for temporary control of the blood supply. Interlocking deep mattress sutures of No. 2 chromic catgut were inserted through the full thickness of the pedicle, entering and emerging on the superior surface, but not tied. With the ends of these sutures held snugly, a wedge shaped incision was made through the pedicle, separating the left and right lobes of the liver. The mattress sutures were then tied and reinforcing sutures were placed over the cut surface of the liver from anterior to posterior edge. These were tied snugly and the enterostomy clamp was removed. Removal of the clamp was followed by bleeding from several vessels, which was promptly controlled by clamping and insertion of additional figure-of-eight sutures. Very little blood was lost from the liver incision. The adhesions between the left lobe and the stomach were then sectioned and bleeding points ligated on the stomach side. Adhesions

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#### CASE REPORTS

**CASE 1**—L. K. K., a white man, aged 73 years, was admitted to Baylor University Hospital, May 27, 1944, complaining of occasional nausea and vomiting with severe pain in the left upper abdomen of four months' duration, frequent belching after meals, and nocturia, one or two times, for several years.

**Present Illness**—The onset was sudden, some time in January, 1944. The patient became nauseated and vomited following the eating of fresh tomatoes. He thought he had "ptomaine poisoning." At the same time, he had a cramping in the epigastrium and noted "rolling movements" and "rumbling" in the abdomen. On feeling the abdomen, the patient noted for the first time a hard lump in the upper abdomen. This mass grew slowly after he first noticed it, and on admission was about twice its original size. No other pain or tenderness was noticed except that occasionally, at frequent intervals (one or two days), a sharp pain beginning in the area of the mass radiated into the left side of the chest and neck. The patient stated that he could move the mass freely. The indigestion continued, and he belched frequently. Bowels moved regularly, there were no clay-colored or tarry stools, and no jaundice.

**Past History**—Questioning showed the cardiovascular system negative, and the respiratory system negative, except for pneumonia seven times during his life, without recurrence in the past fifteen years. There was no additional history of chest pain. Gastrointestinal system was negative, until the present illness. In the genitourinary system, there was nocturia one to two times, no day frequency, burning, or urgency. Extremities were negative. He had fracture of the left clavicle eighteen years before.

The patient led the active outdoor life of a farmer. Fifty years before, he had been bitten by a tarantula on the left cheek. This was followed by marked swelling of the face, which was treated by multiple incisions. Since that time, he had paralysis of the lower left side of the face.

**Family History**—The patient did not remember about grandparents, but both mother and father died of "heart disease." Two brothers and a sister were living.

to the omentum were likewise sectioned and ligated. This allowed removal of the left lobe from the abdominal cavity. The wound was closed with continuous catgut sutures in the peritoneum, interrupted figure-of-eight steel alloy sutures in the fascial layers and rectus sheath. The skin was closed with continuous vertical mattress sutures of cotton. No drains were used.

*Postoperative Course*—Following operation, the patient's condition was good. Temperature reached 101° F. But returned to normal on the third postoperative day and remained so until the sixth postoperative day, at which time the temperature rose to 100.2° F. At this time the patient began to complain of aching pain and tenderness in the calves of both legs, and showed signs of mild thrombophlebitis. The temperature reached 100 to 100.4° F. from the sixth to the sixteenth postoperative days. The thrombophlebitis gradually subsided without further complications. On the eighth postoperative day, the patient was allowed to be up in a wheel chair and was discharged in good condition on the twenty third postoperative day. Elastic stockings relieved the pain in the legs, which were only slightly swollen. His



Fig 3 (Case 1)—Photomicrograph of hepatoma.

course since discharge from the hospital has been quite satisfactory. No abscess has developed although the legs still swell moderately after he has been up for a few hours. His chief complaint now is that he is not allowed to ride horseback, or to help in the fields. Except for a slight bulge in the linea alba at the angle of the incision, the wound is firmly healed. He was last examined on March 15, 1940.

*Pathologic Report*—A pathologic report was made on the liver, June 2, 1941. The specimen consisted of a large liver mass measuring 17 by 18 by 5.5 cm. It was covered by a thin smooth capsule on one side. The omentum was attached to the outer surface of the liver. The greater part of the mass was yellowish in color and contained blood vessels which could be seen. There was a small portion of the mass measuring 10 by 2 by 2 cm. which looked like fairly normal liver. On section the mass was composed of soft fragile grayish-yellow tumor tissue in which were multiple hemorrhagic areas. There were several small

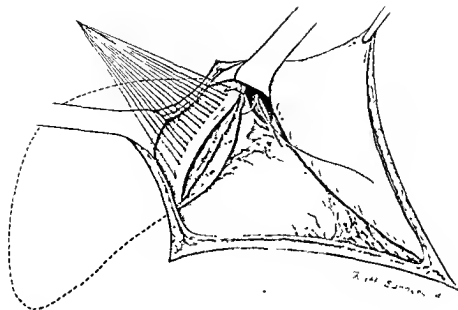


Fig 1 (Case 1) —Resection of left lobe of the liver, mattress sutures are placed but not tied until the pedicle is cut through and the edges of the defect are approximated

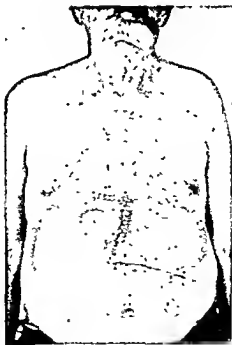


Fig 2 (Case 1) —Photograph of patient showing healed L-shaped scar dotted lines outline liver with tumor.

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*Postoperative Course*—Following operation, the patient's condition was good. Temperature reached 101° F. But returned to normal on the third postoperative day and remained so until the sixth postoperative day, at which time the temperature rose to 100.2° F. At this time the patient began to complain of aching pain and tenderness in the calves of both legs, and showed signs of mild thrombophlebitis. The temperature reached 100 to 100.4° F. from the sixth to the sixteenth postoperative days. The thrombophlebitis gradually subsided without further complications. On the eighth postoperative day, the patient was allowed to be up in a wheel chair and was discharged in good condition on the twenty third postoperative day. Elastic stockings relieved the pain in the legs, which were only slightly swollen. His

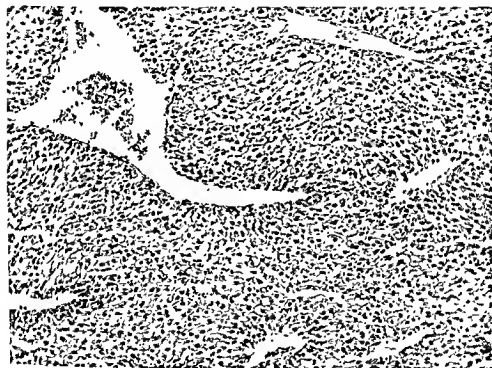


FIG. 3 (Case 1)—Photomicrograph of hepatoma.

course since discharge from the hospital has been quite satisfactory. No ascites has developed although the legs still swell moderately after he has been up for a few hours. His chief complaint now is that he is not allowed to ride horseback, or to help in the fields. Except for a slight bulge in the linea alba at the angle of the incision, the wound is firmly healed. He was last examined on March 15, 1946.

*Pathologic Report*—A pathologic report was made on the liver, June 2, 1944. The specimen consisted of a large liver mass measuring 17 by 18 by 8.5 cm. It was covered by a thin smooth capsule on one side. The omentum was attached to the outer surface of the liver. The greater part of the mass was yellowish in color and contained blood vessels which could be seen. There was a small portion of the mass measuring 10 by 5 by 3 cm which looked like fairly normal liver. On section, the mass was composed of soft fragile grayish yellow tumor tissue in which were multiple hemorrhagic areas. There were several small

arteries filled with light yellow mucous material. The lumen in many places was so soft that it appeared indistinct. There were many white strands which divided the tumor tissue into large lobules. The tumor tissue stopped abruptly where the normal liver tissue began. The cut surface when the liver was removed measured 10.5 cm. in length by 6 cm. The cut surface was composed of tumor tissue. Surface of the mass was not undulated.

Examination of sections of liver showed areas of relatively normal liver tissue on one side with both tumor and tissue on the other and a grading of fibrous connective tissue particularly in the tumor cells in between. The relatively normal tumor tissue was markedly hyaline. The liver cords showed moderate swelling and there was even some variation in the chromatin content of the nuclei of the cells. The bile capillaries and ducts were well distended but the wall was lined by simple columnar epithelium which was regular. There was no invasion of fibrous connective tissue to any great extent in the periportal areas or within the central portions of the lobules which would denote cirrhosis. The fibrous connective tissue in between the relatively normal and tumor masses appeared to be an atypical part of the tumor tissue in appearance. There was a sharp or fairly sharp delineation between the fibrous connective tissue along one side of it. The tumor tissue was composed of cords of cells which had a rather odd appearance, in that they were composed of rather large amounts of hyaline staining material with relatively small round or oval, at times somewhat granular basophilic nuclei which varied only slightly in size, shape, and chromatin content. The cells were fairly regular. Numerous small blood vessels were seen accompanying the tumor formation. The definite differentiation by secretion of bile was not definitely encountered. Mitotic and necrotic figures were seen.

*Diagnosis*—The diagnosis was massive hyaline, relatively benign.

*Case 2*—A. M. M., white male, aged 7 years, was admitted to Texas Children's Hospital, March 12, 1915, with complaints of mass in the upper abdomen for five weeks, vomiting of breakfast two or three times a week, for twelve days, increasing irritability for three or four weeks.

*Present Illness*—On Feb. 26, 1915, the child was taken to the family physician in Thinein, Okla., because he was becoming "just lalled." The large mass was found and the patient sent to Texas Children's Hospital in Dallas. He had been vomiting after breakfast two or three times for the past twelve days, had become increasingly irritable and paler, and in the preceding few weeks had complained of pain in the epigastrium. He had gained weight. There was no hiccups and no fatty stools. The stools were brown and soft, usually one a day. Family history and past history were essentially negative.

*Physical Examination*—The patient was a well-nourished, well-developed, pale, white male child, lying quietly in bed, not acutely ill. The head and neck were not abnormal. Eyes, ears, nose, and throat were not abnormal except for pale mucous membranes. Chest expansion was equal, breath sounds were satisfactory; the point of maximal impulse was the fifth intercostal space, just outside the left midclavicular line. In the heart there were no murmurs or arrhythmia, the rate at the apex was 80, blood pressure 90/70. The abdomen was distended, and there was a round, smooth, nontender, hard mass occupying the right right three-fourths of the abdomen that moved with respiration. This mass appeared to be attached to or part of the liver. The liver could not be outlined as such. The kidneys and spleen were not palpable. In the rectum no masses were palpated. Glandular system contained no lymphadenopathy. The genitals were normal, as were the extremities. The child was pale, but otherwise not abnormal. Reflexes were physiologic and equal.

*Laboratory Studies*—Blood count on March 17, 1915, revealed red blood cells, 4,620,000; hemoglobin, 87; white blood cells, 11,200; polymorphonuclears, 67 (bands, 1; segmented, 6); lymphocytes, 30; monocytes, 3. Urinalysis reaction was acid; albumin; red blood cells were rare; sugar was negative; casts were negative.

Laboratory tests made by the family physician before admission to hospital were as follows: Feb. 19, 1915, red blood cells, 4,820,000; white blood cells, 18,000; hemoglobin, 86 per cent; 11.5 Gm.; stab cells, 2 per cent; segmented, 41 per cent; lymphocytes, 50 per cent; monocytes, 2 per cent; eosinophiles, 1 per cent; myelocytes, 1 per cent; marked anisocytosis.

moderate poikilocytosis. Sedimentation rate was 20 mm, fragility test 0.4 to 0.28, icterus index 6.4; packed cells 40 per cent, volume index 44, color index 68; saturation index 1.6. On Feb. 23, 1945, the urine was negative and there was no bile. Feces showed no fat droplets. There were the usual vegetable cells and fibers and starch granules. Muscle fibers were rare; no ova or parasites. Occult blood was found, benzidine test was two plus. There was no guaiac; bile was negative. March 5, 1945, red blood cells were 4,120,000, hemoglobin, 56 per cent; sedimentation rate was 50 mm.

### Operative Record

*First Operation*—March 15, 1945, exploration and biopsy of liver tumor were carried out.

*Findings*—A left upper rectus muscle splitting incision was made. Upon opening the abdomen, the large, palpable mass proved to be a tumor of the liver, which occupied almost

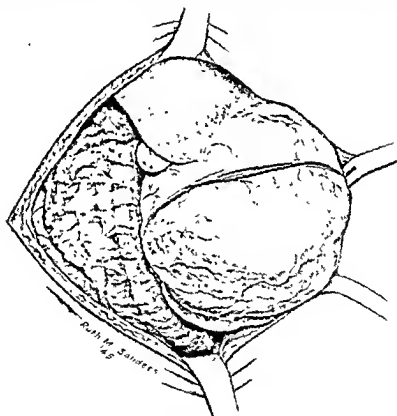


Fig. 4 (Case 2)—Massive hepatoma replacing most of left lobe and invading right lobe, sutures show site of biopsy.

the entire upper half of the abdominal cavity. This tumor was spheroidal in shape. It had replaced almost the entire left lobe of the liver and a large part of the right lobe. There was a narrow fringe of liver tissue about 2 cm. wide, attached to the tumor along its left margin, and a thin layer of liver tissue representing the remaining portion of the left lobe could be palpated behind the tumor. The tumor compressed the right lobe against the right abdominal wall and invaded its substance deeply. The presenting surface of the tumor was a mottled, grayish red in color and was covered by a fairly thick capsule which contained





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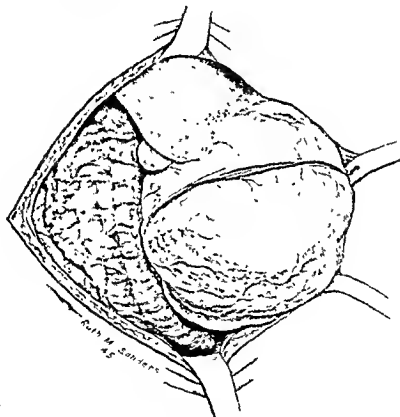


Fig 4 (Case 2)—Massive hepatoma replacing most of left lobe and invading right lobe. sutures show site of biopsy

the entire upper half of the abdominal cavity. This tumor was spherical in shape. It had replaced almost the entire left lobe of the liver and a large part of the right lobe. There was a narrow fringe of liver tissue about 2 cm wide, attached to the tumor along its left margin, and a thin layer of liver tissue representing the remaining portion of the left lobe could be palpated behind the tumor. The tumor compressed the right lobe against the right abdominal wall and invaded its substance deeply. The presenting surface of the tumor was a mottled, grayish red in color and was covered by a fairly thick capsule which contained

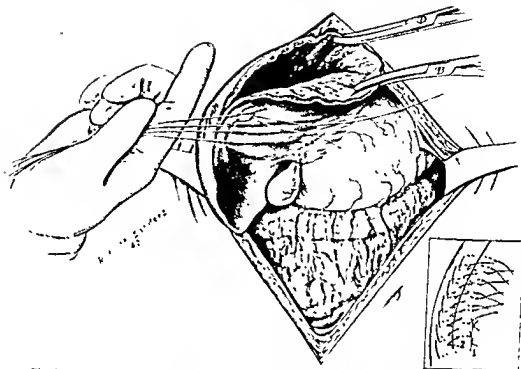
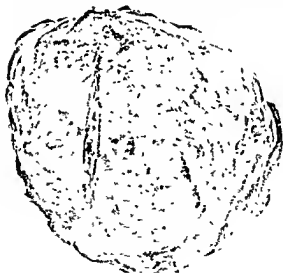


Fig 5 (Case 2) —After tumor has been enucleated margins of left and right lobe remnants are approximated with interlocking mattress sutures and a continuous suture



numerous anastomosing venous channels. The remnant of the right lobe contained a small, raised, grayish area on the anterosuperior surface which was separated from the margin of the tumor. Upon section, this area had the appearance of essentially normal liver tissue. The gall bladder was normal in size and color, but was displaced somewhat toward the right, together with the bile ducts. There was a very thin layer of liver tissue between the tumor and the portal fissure. The stomach was displaced downward and to the left, but was essentially normal in appearance. The spleen was normal.

*What Was Done.*—After thorough examination of the liver and the tumor, resection of the tumor seemed impractical. A biopsy was taken from the anterior surface of the tumor mass, and bleeding was controlled by a series of interlocking mattress sutures of cotton which were placed before the specimen was removed to allow insertion of a series of interrupted sutures, approximating the edges of the defect. The wound was closed in layers with cut drains, using continuous catgut in the peritoneum, interrupted figure-of-eight cotton sutures in the anterior rectus sheath, and continuous vertical mattress suture of cotton in the skin.

### Pathologic Report.—

*Gross examination.*—The specimen consisted of a small bit of tissue measuring 1 by 0.5 by 0.2 cm. The surface was covered with a thick capsule, and beneath this the tissue was firm and yellowish brown in color, resembling fatty liver tissue.

*Microscopic examination.*—The section stained with hematoxylin and eosin revealed tumor tissue bordered on one side by a thick fibrous capsule. Beneath the capsule there was an area containing numerous bile ducts and foci of hepatic parenchymal cells. This area was separated from the main body of the tumor by a thin fibrous band. The main body of the tumor was composed of cords of large cells resembling liver parenchyma cells which were growing in orderly fashion, but not in well-developed lobules. These cells showed marked fatty metamorphosis. In a few areas small bile thrombi could be seen beneath these cells.

*Pathologic diagnosis.*—The diagnosis was benign hepatoma. Recovery from this operation was uneventful. A diagnosis of encapsulated hepatoma was made from the biopsy specimen, and an attempt to resect it was decided upon.

*Second Operation.*—On March 26, 1915, resection of the hepatoma was carried out.

*Findings.*—The findings were as described at the previous exploratory operation, March 25, 1915, there were no adhesions to the wound where the biopsy was taken.

*What Was Done.*—A long, right rectus, muscle-splitting incision was made, paralleling the healing incision to the left. At the upper end, the new incision was extended by section of the costochondral cartilage up to the margin of the sternum. The falciform and coronary ligaments of the liver were sectioned and ligated with cotton. Several large blood vessels, both arteries and veins entering the tumor on its superior surface, were clamped, sectioned, and ligated. Beginning at the antero-inferior margin of the tumor where it invaded the substance of the right lobe, a line of cleavage was established by incising the outer layers of the capsule of the tumor. This line of cleavage was developed laterally and downward toward the anterior margin of the liver, and paired clamps were placed in succession along the margin of the liver tissue about 2 cm. from the tumor. The liver tissue and the outer layer of the split tumor capsule were sectioned together between the clamps which included most of the blood vessels entering the tumor. This procedure was continued around the entire circumference of the tumor, passing from the right lobe to the left lobe in the portal fissure. The tumor mass, together with the attached portions of the liver margins, was then quickly evacuated and the resulting cavity filled with a large, moist pack. Hemorrhage was quite successfully controlled by this procedure. After compression for about five minutes, the pack was gradually withdrawn and the thin shell of liver tissue representing the posterior remnant of the left lobe was tightly compressed against the remaining right lobe. The cut margins of liver which were still retained in the hemostatic forceps originally applied were then sutured together by interlocking, deep, mattress sutures of No. 0 chromic catgut. These sutures entered the liver substance about 2 cm. back from the cut edges. The clamps were then removed and a few bleeding points secured with additional mattress sutures. The edges of the defect were then more closely approximated with a continuous suture of No. 0 chromic catgut. It

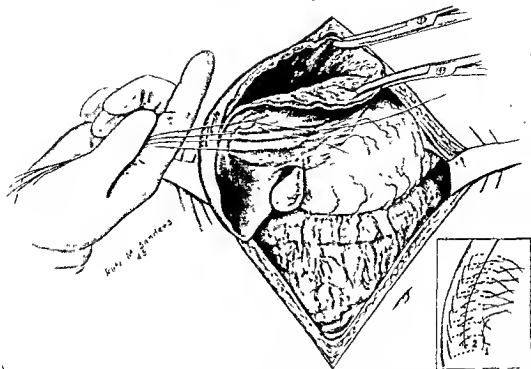


Fig 5 (Case 2) —After tumor has been enucleated margins of left and right lobe remnants are approximated with interlocking mattress sutures and a continuous suture

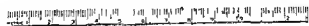
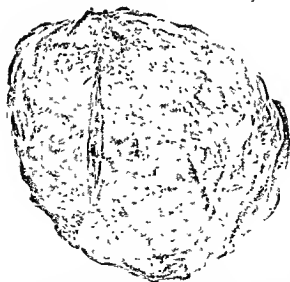


Fig 6 (Case 2) —Tumor after removal

numerous non-tumorous venous channels. The remnant of the right lobe contained a small, raised, grayish area on the anterosuperior surface which was separated from the margin of the tumor. Upon section, this area had the appearance of essentially normal liver tissue. The gall bladder was normal in size and color, but was displaced somewhat toward the right, together with the bile ducts. There was a very thin layer of liver tissue between the tumor and the portal fissure. The stomach was displaced downward and to the left, but was essentially normal in appearance. The spleen was normal.

*What Was Done.*—After thorough examination of the liver and the tumor, resection of the tumor seemed imperative. A biopsy was taken from the anterior surface of the tumor mass, and bleeding was controlled by a series of interlocking mattress sutures of cotton which were placed before the specimen was removed to allow insertion of a series of interrupted sutures, approximating the edges of the defect. The wound was closed in layers with cat gut, using continuous catgut in the peritoneum, interrupted figure-of-eight cotton sutures in the anterior rectus sheath and continuous vertical mattress suture of cotton in the skin.

#### *Pathologic Report.*

*Gross examination.* The specimen consisted of a small bit of tissue measuring 1 by 0.5 by 0.2 cm. The surface was covered with a thick capsule, and beneath this the tissue was firm and yellowish brown in color, resembling fatty liver tissue.

*Microscopic examination.* The sections stained with hematoxylin and eosin revealed tumor tissue bordered on one side by a thick fibrous capsule. Beneath the capsule there was an area containing numerous bile ducts and foci of hepatic parenchymal cells. This area was separated from the main body of the tumor by a thin fibrous band. The main body of the tumor was composed of cords of large cells resembling liver parenchymal cells which were growing in orderly fashion but not in well-developed lobules. These cells showed marked fatty metamorphosis. In a few areas small bile ducts could be seen beneath these cells.

*Pathologic diagnosis.* The diagnosis was large hepatoma. Recovery from this operation was uneventful. A diagnosis of encapsulated hepatoma was made from the biopsy specimen, and an attempt to resect it was decided upon.

*Second Operation.*—On Mar 6, 1915, resection of the hepatoma was carried out.

*Findings.*—The findings were as described at the previous exploratory operation. March 13, 1915, there were no adhesions to the wound where the biopsy was taken.

*What Was Done.* A long, right rectus muscle-splitting incision was made, paralleling the healing incision to the left. At the upper end the new incision was extended by section of the costochondral cartilage up to the margin of the sternum. The falciform and coronary ligaments of the liver were sectioned and ligated with cotton. Several large blood vessels, both arteries and veins entering the tumor on its superior surface, were clamped, sectioned, and ligated. Beginning at the anterosuperior margin of the tumor where it invaded the substance of the right lobe, a line of cleavage was established by incising the outer layers of the capsule of the tumor. This line of cleavage was developed laterally and downward toward the anterior margin of the liver, and paired clamps were placed in succession along the margin of the liver tissue about 2 cm from the tumor. The liver tissue and the outer layer of the split tumor capsule were sectioned together between the clamps which included most of the blood vessels entering the tumor. This procedure was continued around the entire circumference of the tumor, passing from the right lobe to the left lobe in the portal fissure. The tumor mass, together with the attached portions of the liver margins, was then quickly evacuated and the resulting cavity filled with a large, moist pack. Hemorrhage was quite successfully controlled by this procedure. After compression for about five minutes, the pack was gradually withdrawn and the thin shell of liver tissue representing the posterior remnant of the left lobe was tightly compressed against the remaining right lobe. The cut margins of liver which were still retained in the hemostatic forceps originally applied were then sutured together by interlocking, deep, mattress sutures of No. 0 chromic catgut. These sutures entered the liver substance about 2 cm back from the cut edges. The clamps were then removed and a few bleeding points secured with additional mattress sutures. The edges of the defect were then more closely approximated with a continuous suture of No. 0 chromic catgut. It



There was marked distention in the abdomen and the liver was three fingerbreadths below the costal margin. The spleen was not felt, there was no fluid wave. The venous pattern was definite with blood flowing away from the umbilicus.

**Laboratory Studies.**—Urinalysis, Oct. 14, 1945, was negative. On Oct. 20, 1945, it was negative except for occasional white blood cells. Blood count Oct. 14, 1945, was hemoglobin, 10.10 Gm.; red blood cells, 4,470,000; white blood cells, 9,200, polymorphonuclears, 51 per cent (bands, 9, segmental, 34, y.8), lymphocytes, 36 per cent, monocytes, 9 per cent, eosinophiles, 4 per cent. On Oct. 16, 1945, hemoglobin was 12.9 Gm., red blood cells, 4,940,000; white blood cells, 13,850; polymorphonuclears, 74 per cent (bands, 10, segmental, 60); lymphocytes, 25 per cent; monocytes 1 per cent.

**Operation.**—Oct. 14, 1945, resection of the anterior margin of the right lobe of the liver containing the tumor was done.

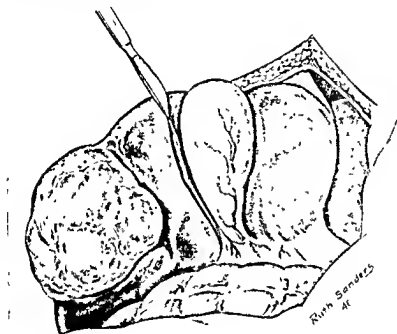


Fig. 7 (Case 3)—Undersurface of liver showing tumor and incision being made in capsule of liver for mobilization of the gall bladder.

**Findings.**—There was a healed scar of a long right upper rectus incision. Upon opening the abdomen, the palpable mass was found to be a tumor embedded in the anterior margin of the right lobe of the liver. The tumor was about 6 cm. in length and 4 to 5 cm. in thickness. Approximately one half its area protruded beyond the line of the liver margin. The tumor was irregular in outline and mottled grayish red in color. Its margin was fairly well defined. The left lateral margin of the tumor was located about 3 cm. from the gall bladder fossa. The gall bladder was normal in size and appearance. The liver was possibly a little enlarged but was otherwise normal in appearance. No other tumor masses could be seen or felt. On the anterior surface of the tumor was a small scar, representing the site of a biopsy previously removed elsewhere. To this scar, a loop of small intestine was densely adherent. The stomach, duodenum, and the remaining portions of the intestinal tract were normal.



Fig. 3. *Procedure*—The scar of the previous operation was excised and lengthened in the upper part to a point 2 cm. below the umbilicus. The rectus muscle was exposed and incised at about its mid point, and the peritoneum was incised. The liver was separated from the surface of the tumor and the gall bladder was inserted with a purse-string (fine catgut) suture. In the center of the tumor mass, the gall bladder was incised almost to its base. To the left, exposing almost the entire gall bladder fossa. A series of No. 0 chromic catgut were placed in a curved line through the liver, enclosing the tumor and a margin of liver tissue about 2.5 cm. wide. The suture on the surface of the liver, penetrated the liver, emerged through

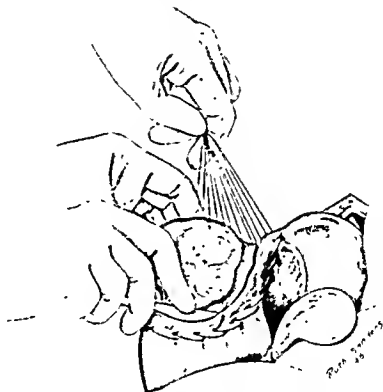


Fig. 3 (Cont.) A series of interlocking mattress sutures placed and held while tumor is resected.

the inferior surface, and then traversed the liver to the superior surface. All mattress sutures were placed and held but not tied until the resection was done. The tumor mass, together with the adjacent margin of liver, was resected in one mass, using a wedge shaped incision so that the margins of the liver could be approximated in a transverse direction. As the incision was made from the left to the right side, the previously placed mattress sutures were drawn tight and tied. Into the troughlike defect remaining on the margin of the liver, masses of fibrin foam, soaked in thrombin solution, were placed. A series of simple sutures were placed across the margins of the incision in the liver and tied in the foam. These sutures resulted in a fairly accurate approximation of the liver, thereby closing the defect. Very little hemorrhage was encountered at

to identify and ligate individual bleeding points. After all sutures were tied, bleeding was completely controlled. The free edge of the omentum was turned upward and secured along the margin of the liver by ligation with the long ends of the second row of catgut sutures, crossing the liver margin. The wound was closed in layers without drains, using fine chromic catgut continuous suture in the peritoneum, interrupted No. 50 cotton sutures in the anterior rectus sheath, and interrupted cotton in the skin.

**Pathologic Report.—**

**Source:** The tumor was from the lower border of the right lobe of the liver.

**Gross examinations** The specimen consisted of a lobular tumor mass, measuring 6 by 3½ by 1 cm., together with a surrounding portion of apparently normal liver. The mass

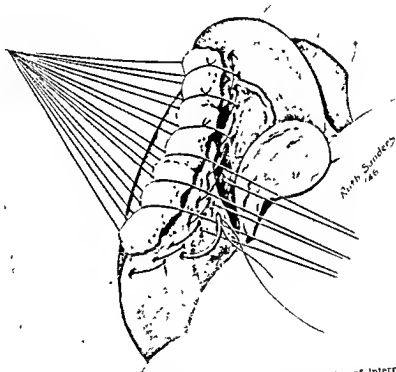


Fig. 9 (Case 3).—Fibrin foam placed in defect and held by second line of interrupted sutures; mattress sutures are tied last.

projected from the liver edge and was covered by what appeared to be a normal extension of the capsule of the liver. It was a smooth, rounded mass with very slight nodulation. There was a mottled, red and light yellow appearance to the surface. There was one area of hemorrhage into the connecting tissues at one extremity of this mass. On cut section there were seen rounded areas 5 to 8 mm. in diameter, separated by apparently fibrous tissue trabeculae. Nodules varied in color from a homogeneous light grey to other nodules which were brownish in appearance. There was no definite gross extension into the apparently normal parenchyma which was attached and surrounded the tumor and there was a suggested, but not definite capsule. The mass was firm throughout and there was no suggestion of necrosis.

*Microscopic examination:* Staining the section with hemotoxylin and eosins revealed, in the tumor mass, cords and sheets of cells separated by fibrous tissue strands which contained moderate numbers of infiltrated small, round, mononuclear cells. The tumor cells had a strong resemblance to normal liver cells, but they were irregular and stained more deeply than the normal liver parenchyma cells. There were occasional multinuclear cells but characteristic large tumor giant cells were not found, nor were mitoses seen in any great frequency. At the border of the tumor small nests of tumor cells were seen and there was no definite demarcation from the surrounding normal liver parenchyma. The latter did not show any increase in fibrous tissue at the portal tracts. The fibrous tissue septa of the tumor itself were extremely vascular, exhibiting many dilated capillaries. In numerous locations masses of tumor cells surrounded blood filled sinuses, from which they were separated only by a thin and sometimes incomplete endothelial lining. In several locations there was seen a tendency for tumor cells in small nests or protuberance of tumor cells to occur in the lumen of these sinuses.

*Pathologic Diagnosis:*—The pathologic diagnosis was primary liver cell adenoma, hepatoma in type, with malignant tendencies.

*Postoperative Diagnosis:*—Postoperative diagnosis was hepatoma, relatively benign.

*Course in Hospital:*—The tumor mass was resected on the third hospital day. Temperature rose to 104° F., and gradually fell to 101° F. by the sixth hospital day. Temperature became normal on the fourteenth hospital day and the patient was discharged on the sixteenth hospital day. Wound-healing reaction was started and discontinued on the second postoperative day. Recovery over a period of two weeks was uneventful. Treatment was symptomatic and supportive.

On April 1, 1946, he was reported to be in perfect health and gaining weight steadily.

#### COMMENT

Our cases represent the age groups at the extremes of life where extensive radical surgery is ordinarily most dangerous. Carefully chosen and skillfully administered anesthesia is, in a large measure, responsible for the successful outcome of the surgical procedure in each case. Of equal importance was the prevention of excessive blood loss. Whole blood was being administered by vein during the course of each operation as a precautionary measure, but relatively little hemorrhage occurred. The plan of placing the line of interlocking mattress sutures before the incision in the liver was made, and exerting traction on all of the untied ends as the incision was made succeeded in compressing the larger vessels whose open ends emerged on the cut surface. Only capillary hemorrhage was, therefore, encountered and this was soon controlled by the approximation of the cut surfaces with the second line of sutures passing over the edges. The use of the enterostomy clamp for compression of the pedicle in the first case was of questionable value.

In the third case, an additional aid was used for control of the capillary bleeding. This was the fibrin foam\* soaked in thrombin solution, applied to the cut surfaces and sutured into the liver wound. Thrombin topical was developed by Tulliek, Seegers, and Warner<sup>13</sup> in 1943, and used as a spray by them to control surface bleeding in skin graft donor sites, bone surfaces, gall bladder beds, mastectomy wounds, etc.

\*The fibrin foam and thrombin used by us was obtained from the Office of Scientific Research and Development, Harvard University, where it is available for clinical experimental use.

Another newly devised substance which would probably serve a similar purpose is absorbable gauze or cotton (oxidized cellulose) \*

The most recently developed hemostatic agent is absorbable gelatin sponge.† A water-soluble gelatin base sponge has been obtained by foaming a specially prepared gelatin solution, which is then air dried in metal forms, and subsequently sterilized for biologic use. The dried product is a light, off-white, non-elastic, tough, porous mold that may be cut into any shape or size. It has no tendency to fragment while being handled. This sponge is not antigenetic. Tests prove it to be absorbed in twenty to thirty days. In use the sponge is dampened with a thrombin solution and the squeezed-out sponge is applied to the bleeding area, where it quickly absorbs blood, which clots upon coming into contact with thrombin.

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\*Prepared in the Research Laboratories of the Eastman Kodak Company, Rochester, N. Y., and sterilized by formaldehyde sterilization by Parker Davis & Company, Detroit, Mich.  
†Prepared by The Upjohn Company, Kalamazoo, Mich.

## A ONE-STAGE PHARYNGOESOPHAGEAL DIVERTICULECTOMY

RAYMOND W. McNALLY, M.D., AND JACOB A. GLASSMAN, M.D., CHICAGO, ILL.

*(From the Departments of Surgery of the Cook County Hospital, Wesley Memorial Hospital, and Cook County Graduate School of Medicine)*

OUR purpose in writing this paper is to present an original method for doing a one-stage pharyngoesophageal diverticulectomy. This method has proved itself to be basically sound because it has been employed successfully for over ten years with great satisfaction to operator and patient.

The surgical treatment of pharyngoesophageal diverticulum has had a varied career. L. von Bergmann and Kocher were among the first to do successful one-stage diverticulectomies. They were outstanding men of their time and their success with this one-stage procedure encouraged many other contemporaries to attempt the same type of operation. Complications followed many of these attempts at one-stage diverticulectomies, and soon there was considerable doubt cast on the wisdom of doing the operation in this way. Leakage from the ligated stump was mentioned as the most common cause of failure. Leakage led to spreading cellulitis along the fascial planes of the neck, and at times it extended even into the mediastinum and involved the lungs, pericardium, and pleura. It was Goldmann who first performed a successful two-stage operation. Halsted, Mayo, Judd, and Lahey later added their individual modifications to the two-stage procedure. However, all these men emphasized the fact that they preferred the two-stage diverticulectomy because it afforded the greatest amount of protection to the mediastinum.

A two-stage operation does not always afford protection against cellulitis and mediastinitis. If leakage occurs it is more likely to come to the surface in the two-stage procedure because the adhesions and walling off of the immediate area about the diverticulum offer a barrier to the extension of infection into the depths of the neck or mediastinum. If one could be assured that the stump left after diverticulectomy would not leak, there would be rarely an occasion for the two-stage operation.

The fact that many of these patients are very poorly nourished makes it imperative that they receive careful preoperative preparation and the necessity for immediate postoperative support is obvious. Immediately preceding surgery a Levine tube is inserted into the stomach via the nasal route. If it is impossible to pass a suction tube due to the tip finding its way into the diverticulum, the tube can be directed easily into the stomach during the operation. We wish to assert ourselves strongly on the subject of when to begin postoperative feedings. It is our belief that patients fed too early (any time before the seventh day) are more likely to develop fistulous tracts. Disruption of the repaired pharyngoesophageal area may be caused if the patient is encouraged to swallow semisolid or solid food at an early date. Even

liquids may cause undue stress on the loosely united wound edges. If consideration is given to parenteral feeding and to the use of the indwelling Levine tube, very few patients will suffer pressure disruption of the repaired defect and their general nourishment will be maintained or improved. Our patients receive their postoperative feedings via the Levine tube after intravenous fluids have been discontinued. They are fed in this manner until the eighth or tenth day after which time the Levine tube is removed and liquid feedings by mouth are instituted.

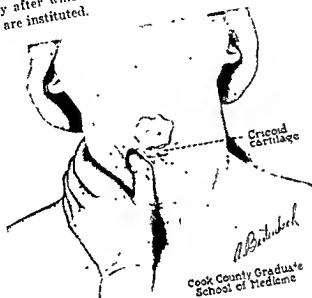


Fig. 1—A method used to determine the position of the diverticulum

The method we employ in one-stage pharyngoesophageal diverticulectomy will be described as it is done, namely, in steps and by the number:

- 1 The incision may be made on either side of the neck along the anterior border of the sternocleidomastoid muscle. It extends about one inch above the level of the cricoid cartilage to one and one-half inches below this level\* (see Fig. 2)
- 2 The fascia along the anterior border of the muscle is divided and the muscle retracted laterally exposing the carotid sheath
- 3 The lateral border of the thyroid gland is exposed and its margin clearly defined
- 4 The carotid sheath, its vessels, and nerve are retracted laterally by ribbon retractor. The thyroid gland and its underlying larynx and trachea are retracted medialward.

\*A simple method for determining the side of the neck on which the diverticulum lies is thereby establishing the probable site for an incision has been described by one of us (McN). It is performed as follows: The patient lying the examiner (sitting or standing) asks the patient to swallow air several times in succession. The examiner's right thumb gently pressed against a point on the left side of the patient's neck anterior to the sternocleidomastoid muscle at a level even with the cricoid cartilage. If the diverticulum happens to be in the neck, it will be forced out by the pressure of the examiner's thumb. Both sides of the neck are tested in this manner.

5 The loose areolar tissue between thyroid and the carotid sheath supports the inferior thyroid artery which usually should be ligated and divided

6. If the lateral margin of the esophagus is now identified, the position of the diverticulum can be established by remembering that its neck is at the

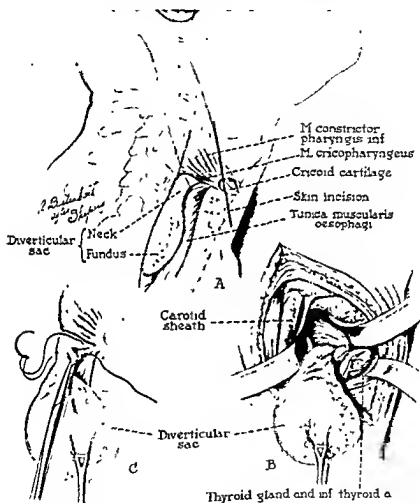


FIG. 2—A, B, and C position of sac and its relation to neighboring structures

level of the cricoid cartilage and its fundus extends downward between the posterior wall of the esophagus and the anterior surface of the prevertebral fascia.

7. Careful traction on the wall of the diverticulum with a Babcock (or similar nontraumatizing forceps) will bring the sac into the more superficial regions of the incision where its size and conformation can be clearly studied.

8. The neck of the sac is now clearly exposed and by lifting gently it will be found that it is possible to rotate the pharyngoesophageal area into direct vision. The extent of the rotation of the esophagus and trachea around the longitudinal axis of these structures has been studied in the living and fresh post-mortem specimens. It is found that with moderate tension this rotation amounts to between 45 and 90 degrees. The maneuver will bring the neck of the sac into a completely visible and accessible position. The recurrent laryngeal nerves are not rendered more vulnerable by this rotation, on the contrary this maneuver permits a better view of the diverticulum. The distal one is not drawn into the field of danger (Fig 3).
9. The muscle fibers of the neck of the diverticulum are now clearly separated from the sac wall with maneuvers which will preserve as many of them as possible because they can be utilized subsequently to reinforce the suture line of the repaired defect (see Fig 4).
10. It is important that the proximity of the recurrent laryngeal nerves be kept in mind (see Fig 3).

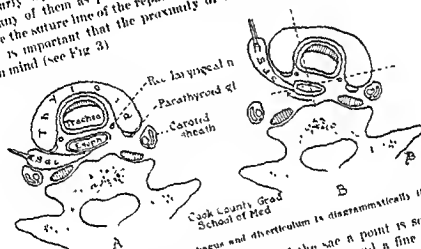


Fig 3. A and B. The mobility of esophagus and diverticulum is diagrammatically illustrated.

11. After a careful survey of the neck of the sac a point is selected at its lateral margin on a level with the cricoid cartilage and a fine forceps is applied transversely. A knife is used to divide the tissue proximal to the jaws of the forceps. This will make the initial opening into the esophagus. The opening is then sutured with one or more interrupted fine silk sutures. A second forceps is applied just beyond the first forceps, care being taken to outline at the same level and maintain the same transverse character of the division. As subsequent forceps are applied and the tissue divided proximally to them the opening in the esophagus is sutured by carefully spaced interrupted sutures until the entire diverticulum has been severed from the pharyngoesophageal junction. This rather methodical clamping, division, and suturing results in a secure closure of the defect in the esophagus without danger of undue narrowing and constriction and without leaving crushed or vitalized tissue in the grasp of the sutures. The well-spaced interrupted sutures bring the mucosa into intimate apposition and secure the holding layers against separation by their distribution of the tension ex-





1 If one wishes to repair or restore the continuity of any hollow viscus, it is not considered beneficial to crush the edges which are expected to unite with one another. We wish to emphasize the importance of suturing freshly divided, nontraumatized tissue in closure of defects of hollow viscera. Tissue that has been crushed lessens the likelihood of a favorable union because nonviable tissue will be included in the suture lines and will offer dead tissue as a site for bacterial growth and extending infection and necrosis. This can hardly help but jeopardize the security of the suture defect and ultimately lead to fistulous formation with all its complications.

2 The use of cautery and escharotics on the edges of defects retards reparative processes even more than crushing of the edges.

3. Continuous sutures have many disadvantages in plastic repairs. A continuous suture strangulates tissues. If one stitch of a continuous chain cuts through it tends to weaken the remaining line. Continuous sutures have a tendency to narrow lumens and to limit the normal elasticity of the region.

4 A further fault would be found in using the same continuous suture as a second line to cover the first. This would have all the disadvantages already described.

5 The use of drains is to be condemned if they act as wicks down to the suture line. The presence of plastic exudate along a sutured line is the first stage in its repair. The removal of this reparative exudate via capillary wick would delay healing and encourage leakage and fistula formation.

#### CONCLUSION

In selected cases a one-stage operation can be done successfully by a technique which we have described. However, there are cases which offer certain obstacles to a one-stage procedure, and these probably can be better handled by a two-stage operation. The surgeon should be guided by his familiarity with the advantages of each type of operation and select the one which is best suited to the particular case in hand. This is obviously a better plan than to limit oneself to the invariable use of one or the other method.

across the posterior wall of the viscus. The diverticulum has been detached from its base in a transverse diameter so that the danger of postoperative stricture formation is greatly lessened (Fig. 4, A, and 2, C).

12 The muscle fibers of the cricopharyngeus and the uppermost fibers of the esophagus are then drawn over the first suture line with interrupted sutures as shown in Fig. 4, B, C, and D.

13 A small soft rubber drain may be inserted down to the lateral margin of the thyroid gland to provide a pathway along which blood or serum may escape. It will likewise form a pathway of easy exitus for any leakage, should it occur.

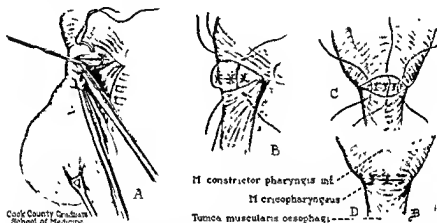


Fig. 4.—A. A method of transverse division of sac and application of interrupted sutures. B, C, and D illustrate the completed suturing of the transverse division of the neck of the diverticulum. Reinforcing sutures through the muscle fibers of cricopharyngeus and muscle fibers of esophagus are also shown.

*In no instance should the wick be carried down to the immediate vicinity of the suture line where it would inhibit the reparative processes by carrying away the plastic exudate from the suture line.*

The following quotation is taken from an article on "Esophageal Diverticula" that appeared in a journal of surgery published during the past year. It seems to us that it is a glaring example of unorthodox surgical procedure.

"Two pairs of Shoemaker colectomy (1) clamps are then applied side by side near, but not too near, to the neck of the pouch. This pouch is now removed by cutting between clamps with the knife or diathermy needle, the line of section between the blades of the remaining clamp being then painted with a little (2) pure carbolic acid. (3) A continuous inverting suture of 2/0 chromic gut is then inserted on a small curved needle over the clamp. The clamp is slid off and the suture at once pulled tight, inverting the edges of the sac. The same suture is then brought back along the whole length as a (4) secondary invaginating stitch and tied to the original end. A few further points of interrupted catgut suture are super added by greater security and the wound closed, leaving (5) a rubber dam drain down to the suture line for three or four days."

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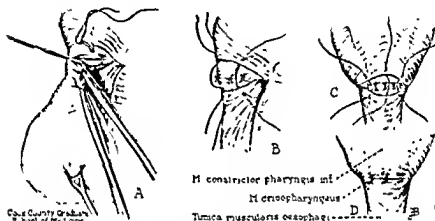


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# SURGICAL MANAGEMENT OF CARCINOMA OF THE RIGHT PORTION OF THE COLON WITH SECONDARY INVOLVEMENT OF THE DUODENUM, INCLUDING DUODENOCOLIC FISTULA: DATA ON EIGHT CASES

MARVIN CALMENSEN, M.D., AND B. MARDEN BLACK, M.D., ROCHESTER, MINN.  
(From the Division of Surgery, Mayo Clinic)

**C**ARCINOMA of the right portion of the colon is a relatively common disease. Secondary involvement of the duodenum by carcinoma of the right portion of the colon is rare. A recent case of carcinoma of the hepatic flexure complicated by a duodenocolic fistula aroused our interest in this subject.

## REPORT OF CASES OF DUODENOCOLIC FISTULA

**CASE 1**—A 32 year old white man entered the Mayo Clinic on Dec. 7, 1945, complaining of epigastric pain of ten months' duration. The pain occurred about one hour after meals and some relief was obtained by drinking milk. Three or four months before admission to the clinic the patient had begun to have low abdominal cramping pain, nausea, and vomiting. Three weeks before admission intractable diarrhea developed. The stools often contained particles of undigested food. The patient had lost 20 pounds (9.1 kilograms) during the three months preceding admission. Appendectomy had been performed in 1941.

Physical examination revealed a soft and tender mass about 6 cm. in diameter to the right midabdomen. The concentration of hemoglobin was 10.9 Gm. per 100 cc. of blood. Erythrocytes numbered 4,600,000 and leucocytes 12,000 in each cubic millimeter of blood. Roentgenologic examination after injection of a barium enema revealed a carcinoma involving the hepatic flexure. Perforation had occurred and a large duodenocolic fistula was present (Fig. 1).

Sulfasuxidine was given for four days preoperatively. Surgical exploration was carried out by one of us (B. M. B.) on Dec. 19, 1945, through a midright rectus incision. There was an extensive lesion of the ascending limb of the hepatic flexure. The lesion had perforated into the duodenum at about the junction of the descending and transverse portions. Although the duodenal involvement was rather extensive, the lesion was still freely movable and there was no evidence of distant metastasis. The right portion of the colon was freed from its lateral peritoneal attachments and detached from the duodenum. The involved portion of the duodenal wall was resected widely. It was fortunate that the portion of the duodenum surrounding the ampulla of Vater was not involved in the malignant process. This made it possible to carry out an adequate resection of the duodenal wall without endangering the entrance of the bile duct and pancreatic duct. The resultant defect in the duodenal wall was closed transversely in the long axis of the duodenum. The terminal 12 to 15 inches (30 to 38 cm.) of ileum, together with the cecum, ascending colon, and approximately one half of the transverse colon, were resected, and the cut ends of the bowel were inverted. Intestinal continuity was reestablished as a side to side antiperistaltic ileocolostomy. Ten grams of sulfathiazole were left in the peritoneal cavity. Closure in layers was performed. The patient was given a transfusion of 500 cc. of citrated blood during the operation.

Convalescence was uneventful and the patient was dismissed from the hospital on the twenty second postoperative day. Roentgenograms taken five weeks after operation showed some changes in the duodenal contour (Fig. 2). The patient has remained well during the four months that have elapsed since the operation.



Fig. 1

Fig. 1—Carcinoma involving the hepatic flexure with perforation and development of a large duodenocolic fistula

Fig. 2—Roentgenograms of stomach and duodenum five weeks following operation showing some postoperative changes in the duodenal contour.

Fig. 2



On microscopic examination there was frank malignant involvement of the duodenum with adenocarcinoma, grade 3 (Hollers' method). The primary lesion measured 7 by 6 by 4 cm. and was situated in the ascending colon near the hepatic flexure. Perforation into the duodenum had developed near the center of the growth. The peritoneum and several regional nodes were involved metastatically.

In one other case only, a duodenocolic fistula resulting from a perforating malignant lesion of the right portion of the colon has been treated at the Mayo Clinic.

**CASE 2**—A 52-year-old white man entered the clinic on June 1, 1936, complaining of diarrhea, weakness, and vague abdominal discomfort of one month's duration. He had lost about 25 pounds (11.1 kilograms) during the past year. The physical examination gave essentially negative results. Roentgenologic examination of the stomach and duodenum showed a duodenocolic fistula involving the proximal part of the second portion of the duodenum. A barium enema of the colon showed a duodenocolic fistula with a large abscess cavity at the site of the communication.

On June 6, 1936, abdominal exploration was performed through a right rectus incision. There was a duodenocolic fistula between the second portion of the duodenum and the transverse colon near the hepatic flexure, as well as an extensive, firm, nodular, partially movable malignant mass which involved the colon and duodenum. Side-to-side ileocolostomy was performed. Four weeks later the abdomen was reexplored. The malignant lesion was very extensive and of doubtful operability. Right hemicolectomy was done, involving removal of the terminal portion of the ileum, the cecum, the ascending colon, and the first part of the transverse colon, including a segment of the anterior wall of the duodenum measuring about 6 by 4 by 3 centimeters. The ends of the ileum and the transverse colon were closed and intestinal continuity was reestablished by means of antiperistaltic side-to-side ileocolostomy. The duodenum was reconstructed. The pathologic specimen consisted of 20 cm. of ileum, the cecum, the ascending colon, and part of the transverse colon. In the hepatic flexure there was an ulcerative adenocarcinoma, grade 2, which had perforated into the duodenum. The tumor involved the peritoneum but there was no glandular involvement.

The postoperative course was stormy, and by the eighth postoperative day it was evident that an external duodenal fistula had developed. Death occurred on the twenty-third postoperative day. Necropsy revealed extensive bilateral bronchopneumonia and an infarct of the right lung. There was no evidence of generalized peritonitis nor any residual carcinoma.

#### ANALYSIS OF DATA

The proximity of the duodenum to the right portion of the colon provides an anatomical basis for the occurrence of secondary involvement of the duodenum by a carcinoma of the colon. The second (retroperitoneal) portion of the duodenum is the segment most frequently involved. The process takes place by direct extension of a perforating lesion of the colon. Acute perforation, which occurs infrequently, may be associated with spreading peritonitis. Usually the process is chronic, with adhesion of the adjacent viscera and the formation of a walled-off region. The extent and duration of the lesion determine whether or not an actual fistulous communication is established between the colon and the duodenum.

Reports of cases of duodenocolic fistula resulting from carcinoma of the colon are few. In 1935 Mindline and Rosenheim<sup>1</sup> stated that they were unable to find in recent literature any case of a fistulous opening between the duodenum and the colon resulting from malignant disease. They reported one

case and subsequently others have been recorded by Saleh,<sup>2</sup> Hubeny and Delano,<sup>3</sup> Feldman,<sup>4</sup> and Linton.<sup>5</sup>

The diagnosis of a duodenocolic fistula is usually made roentgenologically. The symptoms do not differ from those of a gastrocolic fistula. Persistent diarrhea and a rapid loss of weight, often accompanied by pain and anemia, are usually present, and the occurrence of fecal vomiting is common. Weber<sup>6</sup> and other observers<sup>2-4</sup> have pointed out that the fistulous communication is demonstrated better and more frequently with a barium enema than with barium given by mouth.

Cases of operable carcinoma of the right portion of the colon complicated by secondary involvement of the duodenum without formation of fistula, while more common than those cases complicated by fistula, are also decidedly rare. In the period of thirty-nine years from 1907 to 1945, inclusive, in approximately 1,400 cases carcinoma of the right portion of the colon was treated surgically at the Mayo Clinic. There were eight cases of carcinoma of the right portion of the colon with perforation onto or into the duodenum. In the two cases previously summarized duodenocolic fistula had developed. In the remaining six cases the duodenum was involved in the malignant process, but there was no actual fistula. Seven of the patients were men and one was a woman. The youngest patient was a woman of 29 years, the oldest a man of 67 years, and the average age was 49.5 years. The average duration of symptoms before operation was 7.6 months.

The primary lesion involved the hepatic flexure of the colon in five cases, and the cecum or ascending colon in three. The second portion of the duodenum was involved in seven cases, the first portion in one case. Both of the duodenocolic fistulas communicated with the second portion of the duodenum. In every case the lesions were large, ulcerative, perforating adenocarcinomas of either grade 2 or 3, using Broders' classification. It was rather surprising to discover that with lesions as extensive as these there was no involvement of lymph nodes in three of the cases. Regional lymph nodes were involved by metastatic carcinoma in the five remaining cases.

*Operative Procedures.*—Dr W. J. Mayo operated on the earliest patient in this series in 1909. He removed a segment of the ascending and transverse colon and re-established continuity of the bowel by means of a side-to-side anastomosis. The carcinoma involved the distal end of the stomach and the first portion of the duodenum. The distal portion of the stomach and the proximal 4 inches (10 cm.) of duodenum were resected in addition to the removal of the colon. This patient lived one year following operation and survived longer following the operation than any other patient in the series. In the remaining seven cases right hemicolectomy and ileocolostomy were performed in each instance. In three of the cases this was done as a two-stage procedure. In these cases ileocolostomy was performed as the first stage and several weeks later the right portion of the colon and terminal ileum were removed as the second stage. In four of the cases the procedure was done in one stage.

With the exception of Mayo's case, local excision and plastic repair (duodenoplasty) were performed in each instance. In one case a portion of the pancreas was also removed.

*Survival Time Following Operation*—Of the eight patients, three died while confined to the hospital following operation. One patient died of generalized peritonitis eight days following operation, one died of a pulmonary infarct and bronchopneumonia twenty-three days following operation, and one died, probably from a pulmonary embolism, three days following operation.

Two patients died eight months following operation, and one patient, previously mentioned, survived one year following segmental resection of the colon with partial gastrectomy and partial duodenectomy. One patient (authors' case) is living and well four months following operation, and one patient is living and well nine months following operation for a recurrent carcinoma of the cecum.

#### COMMENT

The review of these cases of carcinoma of the colon complicated by involvement of the duodenum was undertaken primarily to determine the feasibility of removing segments of the duodenal wall and to study the course of these patients following this procedure. The complication is so unusual that the study would seem warranted. Worthy of mention is the fact that the retroperitoneal portion of the duodenum may be mobilized and subjected to local excision without undue risk or danger of formation of a fistula. As previously mentioned, a fistula occurred in only one of the seven cases in which excision and duodenoplasty were performed. When the second portion of the duodenum is subjected to surgical intervention it is extremely important to safeguard the ampullary structures in dissection. Obviously, if these structures are involved in the malignant process a more radical procedure may be indicated.

Linton<sup>8</sup> has reported two cases of carcinoma of the transverse colon with duodenocolic fistula in which a two stage procedure was carried out, the second stage being a more radical procedure such as is done for carcinoma in the head of the pancreas. In the first stage the stomach and the ileum were transected and gastrojejunostomy and ileotransverse colostomy were performed. The second stage consisted of a block extirpation of the primary growth with the involved organs (right hemicolectomy and resection of the distal half of the stomach, duodenum, and head of the pancreas with reestablishment of gastrointestinal and biliary continuity). It cannot be denied that this is a more radical procedure and is in keeping with present concepts of surgical treatment of carcinoma in general. However, in neither case was the patient cured by the operation. One patient died eight months after operation and the other had a metastatic mass in the abdomen eight months after operation. The decision as to which procedure to perform, and as to whether the procedure should be in one stage or in two stages, must depend on the individual circumstances present in each case. The age and general condition of the patient, the extent of the lesion, and the involvement of con-

tigious structures must govern the surgeon in his plan of attack. In recent years, with the adjuvants of preoperative preparation of patients with sulfasuxidine, the intraperitoneal use of sulfonamides, and blood transfusions and penicillin at their disposal, surgeons are tending more and more to do one-stage procedures in many instances of major surgical undertakings which formerly were done in two stages.

#### SUMMARY

In eight cases, from 1907 to 1945, inclusive, carcinoma of the right portion of the colon, with secondary malignant involvement of the duodenum, has been treated surgically at the Mayo Clinic. The second portion of the duodenum was involved in seven of the eight cases, the first portion in one case. In two of the cases involvement of the duodenum took the form of a duodenocolic fistula. Duodenocolic fistula secondary to malignant disease of the colon is a rare entity and occurs only when the disease is advanced. The lesions were removed in one or in two stages. In seven of the eight cases right hemicolectomy, with local excision of a portion of the duodenal wall and duodenoplasty, was carried out. In the remaining case segmental resection of the colon, with partial gastrectomy and partial duodenectomy, was done. The risk of operation in these cases is high. There were three deaths in the hospital in the eight cases. The prognosis in such cases is unfavorable. The longest survival period following operation was one year.

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## THE McARTHUR OPERATION FOR INGUINAL HERNIA

FREDRICK CHRISTOPHER, M.D.,\* AND OTTO J. PENNA, M.D.†  
EVANSTON, ILL.

ATTEMPTS to evaluate the different methods of inguinal herniorrhaphy are difficult to make, and many pitfalls are encountered. Not only must the type of hernia, the type of operation, the experience of the surgeon, the type of suture material, the age and occupation of the patient, and the time of ambulation be considered, but also the care and accuracy with which the follow-up studies are made. Unfortunately, in some published series, part of the follow-up data are based upon mailed replies to questionnaires and not on actual examinations.

For the last four years the senior author and his surgical residents have employed uniformly the McArthur technique for all herniorrhaphies except in children. Indirect and direct hernias have all been treated identically. Since January, 1937, but principally between February, 1941, and November, 1945, the McArthur procedure has been carried out 202 times (including the bilateral hernias), 161 of the operations being done by the senior author and 41 by the surgical residents.

The McArthur technique as employed by us is as follows. Silk is used throughout. The sac is transfixed and ligated and the stump fixed or allowed to retract under the internal oblique muscle. Occasionally, in small direct hernias the sac is unopened. The cord is transplanted. A fascial suture about 4 to 10 mm wide and about 12 to 15 cm long is prepared from the mesial border of the split aponeurosis of the external oblique muscle. The fascial suture is left attached at the symphysis pubis. By means of this fascial strip, the "conjoined tendon" and usually the transversalis fascia are approximated firmly to the inguinal ligament by continuous suture. The suture is doubled back from the cord for a few bites, and the end is securely anchored with five or six interrupted No. 00 silk sutures. With the cord still transplanted, the mesial border of the split aponeurosis of the external oblique is sutured with interrupted silk sutures to the inguinal ligament, and the outer layer of the aponeurosis is imbricated over it. The cord is left immediately beneath the skin and subcutaneous fat. The aponeurosis of the external oblique is imbricated above the cord, the lateral flap being uppermost. The opening for the cord is made as small as will permit a Kocher director to be passed easily through it in addition to the cord. For the last thirteen months the patients have been encouraged to get out of bed by the first or second postoperative day and have been sent home on the fourth to eighth day.

The McArthur operation was first described in 1901.<sup>1</sup> In addition to the surgeons listed in Table I, the procedure has been warmly endorsed by Bissard<sup>2</sup> and by Sachs,<sup>3</sup> the latter employing two fascial sutures. Joyce<sup>4</sup> has used the McArthur operation in about 10 per cent of his cases.<sup>5</sup> Excellent illustrations of the method may be found in the papers by Bissard<sup>2</sup> and by Ryan.<sup>6</sup>

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\*Associate Professor of Surgery Northwestern University Medical School. Chief Surgeon, Evanston Hospital.

†Resident in Surgery, Evanston Hospital.

In the series of cases here reported, there were 71 indirect hernias, 31 direct hernias, 18 hernias with type not recorded, 7 recurrent hernias, 2 direct-indirect hernias, and 1 hernia without a sac in a total of 112 patients. There were 106 men and 6 women. The average age was 46.6 years, the extremes being 19 and 75 years. Over 175 letters were written requesting the patients to report for follow-up examination. A total of 112 patients actually appeared and were examined by the senior author. The average interval between the time of operation and the follow-up examination was 24.2 months, the extremes being 3 months and 61 months. There were two deaths, one from pulmonary thrombosis and one from pulmonary embolism. There were three cases in which infection developed, and in one of these cases the hernia recurred. Among the seventy-two patients who failed to report for follow-up examination, one was known to have had a recurrence.

TABLE I. MCARTHUR OPERATION

AUTHOR	NUMBER OF OPERATIONS	NUMBER OF RECURRENCES	PERCENTAGE OF RECURRENCES
Lyle <sup>8</sup>	132	8	6.0
Cattell and Anderson <sup>9</sup>	20	1	5.0
Robins <sup>10</sup> (direct only)	27	0	0.0
McCloskey and Lehman <sup>11</sup>	82	3	3.6
McLaughlin <sup>12</sup>	90	0	0.0
Burton <sup>13</sup>	132	6	4.5
Ryan <sup>6</sup>	92	0	0.0
Christopher and Penna	130	4	3.1
Total	705	22	3.1

TABLE II. GALLIE OPERATION

AUTHOR	NUMBER OF OPERATIONS	NUMBER OF RECURRENCES	PERCENTAGE OF RECURRENCES
Cattell and Anderson <sup>9</sup>	125	7	5.6
Burdick and co workers <sup>14</sup>	975	244	25.1
Keynes <sup>15</sup>	35	0	0.0
Gray <sup>16</sup>	54	4	7.4
Total	1,189	295	24.8

In Tables I to III, unless the quoted series is for direct hernias only, the direct and indirect hernias are grouped together. It is well known that the incidence of recurrence of direct hernia is several times greater than that of indirect hernia. To include them together does not invalidate the basis of comparison. In Table I are shown the results in the McArthur operation; in Table II, in the Gallie fascial transplant method, and in Table III, in a representative group of other methods.

The cases in which recurrence occurred are abstracted as follows:

CASE 1.—Dr R. S., a white man, aged 53 years, had an indirect hernia. He was operated upon June 15, 1942. There was a recurrence six months later. The second operation was done on June 21, 1943. There was no recurrence following the second operation (follow-up after forty-five months).

CASE 2.—D. D., a white man, aged 67 years, had a large direct hernia with cecum attached to the sac. Operation was done on May 10, 1943. On examination thirty-four months after operation a recurrence with a 3 cm. sac was found. Operation for recurrence was not advised.

TABLE III. NONFUSCUM OPERATIONS

AUTHOR	NUMBER OF OPERATIONS	NUMBER OF RECURRENTS	PERCENTAGE OF RECURRENTS
Erdman <sup>17</sup>	978	72	7.3
Ostfeld <sup>18</sup>	586	31	5.4
Fallis <sup>19</sup>	800	66	8.5
Parsons <sup>20</sup> (chromic gut)	244	31	12.7
Parsons <sup>20</sup> (silk)	458	16	3.5
Shelley <sup>21</sup>	2,126	188	8.8
Blanchard <sup>22</sup>	366	23	6.8
Stein <sup>23</sup>	101	5	4.9
Maingot <sup>24</sup>	500	15	3.0
DeCourcy <sup>25</sup>	220	8	3.6
Total	6,379	457	7.1

CASE 3—A B, a white man, aged 47 years, had a right direct hernia. Operation on Oct. 30, 1941, was followed by wound infection with abscess which required incision and drainage (25 cc of pus). Ten days before this operation the patient sustained a perforation of the terminal ileum from muscular effort. The perforation was repaired through a right rectus incision on the day of the accident. It is quite probable that a longer interval after the operation at which peritonitis was found should have been allowed before the hernia operation was undertaken. Operation was done for recurrence (above the external ring) on Jun. 22, 1943. No recurrence was noted at a follow up examination twenty-nine months after the second operation.

CASE 4—W R, a white man, aged 61 years, had an indirect hernia. A slight recurrence above the external ring was noted ten months after operation. The condition was unchanged thirty-nine months after operation. The patient was wearing a truss.

## SUMMARY

In a series of 130 hernioplasties for indirect and direct inguinal hernia in which the McArthur method of operation was performed, the incidence of recurrence was 3.1 per cent.

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# INCISIONAL HERNIA, OPERATIVE TECHNIQUE

DANIEL V. THOMPSON, M.D.,\* PROVIDENCE, R. I.

**A** SURGICAL technique for repair of incisional hernia is presented which reduces operative time, reduces tissue dissection, and gives a firm repair to the hernia. It will also reduce the incidence of postoperative collections of serum because less dissection of the subcutaneous fat is necessary.

An elliptical skin incision is made including the old scar and redundant skin (Fig. 1). Care is taken not to open into the sac while the scar is excised. If the peritoneal cavity is accidentally entered, it is sutured immediately. The left hand then invaginates the sac on one side, coming to rest against the hernial ring. With the hand in this position, an incision is made through the fat about 2 cm. from the edge of the ring (Fig. 2). This incision goes straight down to clean fascia. If the fat pad over the hernial ring is thick, this incision through the fat is made tangentially. The blade facing down and out, so that a relatively thin layer of fat is left over the edge and adjacent area of the ring. In early cases at this hospital, the incision in the fat was made straight down and subsequently trimmed down if invagination of the fat over the sac was difficult. By cutting tangentially when the fat pad is thick, this extra step is eliminated.

With the hand invaginating the hernial sac supporting the wall, the fascia is rapidly cleared of fat for an area of about 4 cm. laterally. An incision is made in the fascia 1 cm. from the medial edge of the fat (Fig. 3). The index finger is inserted in this incision. The fascia here is far enough from the edge of the hernial ring to be free of adhesions and lifts easily. The blade of a pair of curved scissors is then inserted along the finger and the fascia is incised as the finger is advanced (Fig. 4). The same procedure is carried out on the other side. A small strip of fascia 1.5 cm. wide is left intact at both ends (Fig. 5, *E* and *F*).

The outer edge of the strip of fascia which surrounds the ring (Fig. 5, *A*) is sutured to the corresponding edge on the other side (Fig. 5, *A'*), thus folding over the sac the subcutaneous fat that overlies this strip (Fig. 6). In this manner, the subcutaneous fat is converted into preperitoneal fat.

The lateral edges of the incised fascia are then sutured together with overlap (*B* to *B'*, Fig. 7).

If the patient is dieted preoperatively and made to lose weight, we have no difficulty in overlapping the edges (*B* and *B'*, Fig. 7). If overlapping is not possible these edges are merely sutured together. If the gap is too large so that this suturing is not possible without undue tension, then fascial transplants can be used to cover the defect over the rectus muscle (Fig. 6).

There is no doubt that a pedicled fascial transplant is more likely to give good wound healing than a free graft from the fascia lata. Wangenstein has given us an excellent method whereby we can close these defects in large hernias. If the hernia is in the lower abdomen, the iliotibial tract

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\*Assistant Surgeon, Rhode Island Hospital.





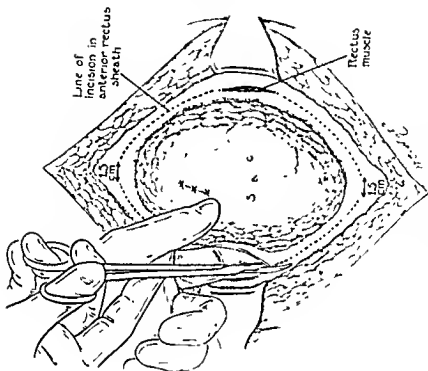


Fig. 4.

An incision is made along this finger cuts the fascia as the finger is pushed along parallel to the ring. The fascia usually lifts easily. A pair of curved

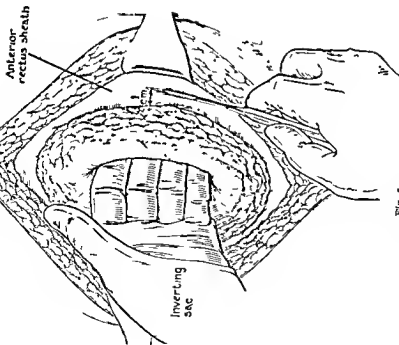


Fig. 3.

is made into the fascia thus exposed. A cuff from the medial fat edge. A suture is inserted under the fascia through the incision just made. The fascia usually lifts easily. A pair of curved

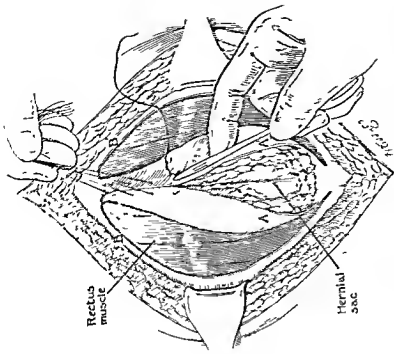


Fig. 5.

The sac is not entirely completely around the ring. An area 1.5 cm. wide is left intact at the upper and lower ends. The sac is shown where the sac was originally open and properly situated. The area of former subcutaneous fat which overlies the hernial ring is shown. With the transposition of nature of the fat, the area of former subcutaneous fat which overlies the hernial ring is shown. The area of former subcutaneous fat which overlies the hernial ring is shown. The area of former subcutaneous fat which overlies the hernial ring is shown.

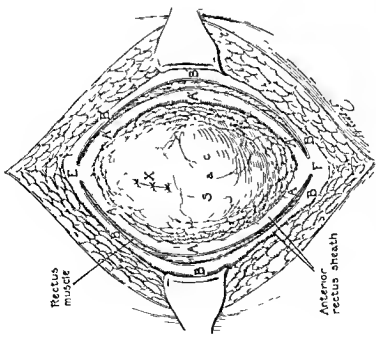


Fig. 6.

The sac is not entirely completely around the ring. An area 1.5 cm. wide is left intact at the upper and lower ends. The sac is shown where the sac was originally open and properly situated. The area of former subcutaneous fat which overlies the hernial ring is shown. With the transposition of nature of the fat, the area of former subcutaneous fat which overlies the hernial ring is shown. The area of former subcutaneous fat which overlies the hernial ring is shown.

and its lateral extensions of fascia lata are brought over Poupart's ligament into the site of the defect.

A defect in the upper abdomen is closed by Waugensteen's technique of swinging up a fascial flap from the lower abdomen and then covering this latter defect with a pedicled iliothoracic tract fascial transplant.

#### DISCUSSION

By leaving the incised fascia attached at two points (*E* and *F*, Fig 5), we do not interrupt its continuity with the main fascial plane. Also, after suture of the edges (*A* to *A'*, Fig 5) we have a solid sling of fascia across the center of the hernial sac (Fig 7). The blood supply seems to be adequate not only

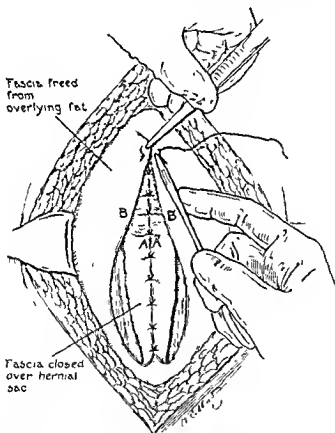


Fig 7—Fascial edge *B* is now sutured to *B'* with overlap thus completing the repair.

for this fascial strip but also for the attached fat that is buried under it. Since none of these patients needed reoperation we cannot say definitely whether this buried fat remained viable as preperitoneal fat or broke down and was replaced by scar tissue. Postoperatively the wounds in this small series healed per primam, except one. This patient, M. M. (Hospital No. 334526), was operated upon June 26, 1940. She had three small defects in the fascia above the main

sac and required dissection and repair of the three small defects before the main defect was repaired with this technique. A moderate amount of serum drained on removal of sutures. However, follow-up study was made until March 26, 1943, when she no longer reported back to the follow-up clinic, and up to that time the scar was firm with no recurrence. In the remaining patients in this small series healing was per primam and there have been no recurrences.

#### SUMMARY

1. A surgical technique for repair of incisional hernia is presented which reduces fat dissection and operative time.
2. This also gives a firm repair of the hernia.

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## ADENOMATOUS GOITER WITHOUT HYPERTHYROIDISM

### SURGICAL VERSUS CONSERVATIVE TREATMENT IN OVER TWO HUNDRED PATIENTS

LIEUTENANT (J.G.) JOSEPH A. BUCKWALTER, USNR, EDWARD L. BESSER, M.D.,  
MANCHESTER, CONN., AND JOHN W. DULIN, M.D., IOWA CITY, IOWA

(From the Department of Surgery, University of Iowa, Iowa City)

**R**EVIEW of the literature relative to the surgical versus the conservative treatment for nontoxic nodular goiter brings to light conflicting opinions on this question. The two schools of thought are represented in many institutions by the surgery department which advocates surgery in these cases and the medical department which advocates conservative treatment. It was this situation which furnished the stimulus for this paper.

There are several possible indications for surgery in nontoxic nodular goiter:

1. Cosmetic reasons. This is an individual consideration and will not be discussed further.

2. Pressure symptoms. This is largely dependent on the size and position of the goiter and is not a controversial subject.

3. Prevention of the development of carcinoma or the fact that carcinoma may already be present and not recognized. Authorities vary in reports as to the incidence of carcinoma in nodular goiters. Recent studies by Cole and associates<sup>1</sup> suggest that it is higher than generally appreciated and they feel that this incidence is a sufficient indication for surgery, particularly if there is a solitary adenoma.

4. Prevention of the development of toxic nodular goiter. It is difficult to ascertain how many people who have a nodular goiter will eventually develop toxic symptoms. It has been estimated that such toxicity develops in about 50 per cent of these patients.<sup>2</sup>

5. The existence of systemic symptoms even though the basal metabolic rate is normal and the patient is not obviously toxic.

This paper will be concerned with the last two indications.

The problem immediately arises as to what is the criteria for deciding whether a given goiter is toxic or nontoxic. If the patient has an elevated basal metabolic rate, nervousness, palpitation, weight loss, increased appetite, etc., the diagnosis of toxic nodular goiter may be made. If, however, a patient with a nodular goiter has a normal basal metabolic rate, but does have symptoms such as those commonly associated with hyperthyroidism, it is difficult to decide whether this is due to the goiter. The border line between nontoxic and toxic nodular goiter is certainly indistinct. Nevertheless, for purposes of coding records, the diagnosis of one condition or the other must be made. In this paper, our interest is in those patients in whom the diagnosis was made of a nontoxic nodular goiter.

TABLE II. SYMPTOMS ON ADMISSION AND ON FOLLOW UP

	ON ADMISSION					ON FOLLOW-UP				
	YES	NO				YES	NO			
	PER CENT	NUMBER OF PATIENTS	PER CENT	NUMBER OF PATIENTS	PER CENT	PER CENT	NUMBER OF PATIENTS	PER CENT	NUMBER OF PATIENTS	PER CENT
<i>Nonoperated</i>										
Nervousness or irritability	81	74	17	15	0	71	63	27	24	2
Palpitation or tachycardia	84	74	16	14	0	65	57	33	29	2
Shortness of breath	73	64	27	24	0	59	52	38	33	3
Weight loss	49	42	52	48	0	29	26	71	63	
<i>Operated</i>										
Nervousness or irritability	25	103	5	6	0	16	17	79	83	6
Palpitation or tachycardia	85	07	15	17	0	21	21	73	72	6
Shortness of breath	96	108	4	4	0	18	20	80	88	2
Weight	54	59	Loss			Gain since operation				
			43	47	0	74	82	25	28	1

7 represents patients who did not know how to answer the particular question

*Palpitation or Tachycardia*—Palpitation or tachycardia was present in 84 per cent of the group not operated upon and in 85 per cent of those operated upon on admission. Of those not operated upon 65 per cent reported that they still had pounding of the heart, while in those operated upon, 73 per cent were completely relieved of this symptom.

*Shortness of Breath*—In the group not operated upon, shortness of breath was noted in 73 per cent of the patients on admission and in those operated upon, in 96 per cent. Of those operated upon, 80 per cent were relieved while 59 per cent of those not operated upon still reported shortness of breath.

*Weight Loss*—Loss of weight was a less frequent symptom. Of the patients not operated upon, 48 per cent reported weight loss on admission and 29 per cent reported continued weight loss at the time of the follow-up. Of those operated upon, 54 per cent reported weight loss before the operation and 82 per cent reported that they had gained weight since the operation.

*Patients' Evaluation of Therapy*—In the group not operated upon, 8 per cent of the patients reported that they had improved, 11 per cent had progression of the symptoms, and 68 per cent reported that their condition was essentially unchanged; 13 per cent were equivocal. Of the patients operated upon, 59 per cent were improved, 9 per cent were worse, and 30 per cent were unchanged; 2 per cent were equivocal.

#### DISCUSSION

There are obvious objections to conclusions that are reached by a questionnaire study of this type. Nevertheless, they do show trends. Our results would

tend to bear out those who contend that the nodular goiter usually referred to as nontoxic is often associated with symptoms of nervousness and irritability, palpitation, tachycardia, and weight loss. These symptoms are present when the basal metabolic rate is within normal limits. On the basis of this study we feel that surgery is indicated in this group of patients and will result in the relief of symptoms present in patients with nontoxic nodular goiters in a significant percentage of cases.

#### SUMMARY

1. Members of the medical and surgical departments in a series of medical schools were contacted relative to policies of management of patients having nontoxic nodular goiters. Replies were summarized.

2. For this study, 374 questionnaires were sent out to patients previously seen at the University of Iowa Hospitals who had been diagnosed as having nontoxic nodular goiters. Two types of questionnaires were used, one type going to those who had not been operated upon and a second type going to those who had been operated upon.

3. At the time of their admission about three-fourths of all these patients with so-called nontoxic nodular goiters suffered from symptoms often associated with hyperthyroidism in spite of normal basal metabolic rates.

4. Thyroidectomy resulted in regression of these symptoms in a large percentage of cases, whereas little change was noted in the group of patients who were not operated upon, after a period of from one to five years.

5. In one to five years after their discharge, 59 per cent of the group of patients who had operation were unimproved while 8 per cent of those not operated upon were improved.

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Many authorities have pointed out that the basal metabolic rate in itself is not a criteria of the toxicity of a goiter. Hertzler,<sup>5</sup> in his recent monograph on thyroid disease, stressed this point and cited his experience with patients on whom follow-up had been carried out for long periods of time and who eventually developed what he called "goiter heart" even though the basal metabolic rate was never found elevated. These patients were greatly improved following thyroidectomy. In 1931, Collier and Arn<sup>6</sup> studied a group of fifty patients who had had a subtotal thyroidectomy during 1927 or 1928. All of these patients had a basal metabolic rate of less than plus 1 prior to operation. A sense of pressure in the neck was present in 44 per cent of these patients. Nervousness was an important symptom in almost every patient. Irritability was associated with this symptom. Palpitation and shortness of breath were complained of by more than one-half of these patients. Other less common symptoms were indigestion, intermittent diarrhea, easy fatigue, and muscular weakness. These authors concluded that nodular goiters associated with basal metabolic rates, in normal and subnormal ranges, can and often do cause systemic symptoms. In most cases these symptoms disappear after the removal of the goiter. Searls<sup>7</sup> in 1936 discussed his experience at the University of California Hospital with a group of patients complaining of nervousness, easy fatigue, palpitation, shortness of breath, and vague gastrointestinal symptoms. These patients were characterized by having a low basal metabolic rate. Removal of the adenomatous goiter resulted in relief of the symptoms in a high percentage of cases. Wetherell<sup>8</sup> pointed out that the use of an elevation in the basal metabolic rate as a criteria for operation in nodular goiter is an unwise practice. In patients having basal metabolic rates ranging from plus 15 to minus 20, in his experience, 85 per cent of the patients suffered from palpitation, about the same percentage suffered from shortness of breath and irritability, and a significant percentage suffered from easy fatigue, excessive dryness of the skin, brittle nails, and cardiac symptoms. He found that cardiac abnormalities were often present. He presented case histories of patients in whom these symptoms were relieved following thyroidectomy. Chesky,<sup>9</sup> in 1939, observed that there was definitely a higher incidence of cardiac abnormalities in a group of patients with nontoxic nodular goiter than in a similar group of patients without a goiter.

There have been very few papers written in opposition to surgical treatment of nontoxic nodular goiter. In 1937, Jackson<sup>10</sup> described 100 cases in which he said needless thyroid surgery had been done. He felt that the surgeon must be certain that the patient is suffering from true hyperthyroidism with its toxic manifestations before he is justified in performing a thyroidectomy. In 1938, Welti and Leven<sup>11</sup> published a paper on useless thyroidectomies.

During the past year, representatives of the surgical and medical departments of other medical schools were contacted in reference to their management of these patients. In a few instances the opinions expressed were those of the individual, while in the rest it represented departmental policies. Twenty-six medical departments expressed the following views: fifteen advised conservative expectant treatment, nine advised surgery in all nodular goiters, and two advised surgery when the patient has reached the age of 35 years. Twenty-four surgical

departments expressed the following views: seventeen advised surgery, five recommended conservative expectant treatment, and two advised surgery when the patient has reached the age of 35 years. There were six instances in which opposing policies existed within the same institution.

#### CLINICAL STUDY OF UNIVERSITY OF IOWA CASES

All histories of patients on whom a diagnosis of nontoxic nodular goiter had been coded during the years 1938 through 1942 and a few from 1943 and 1944 were studied. These included indigent and private patients. Cases in which there were associated significant disease processes were excluded. All of the patients studied had basal metabolic rates considered to be within normal limits, although it must be admitted that some of these were single determinations. It was the general policy of the medical department not to advise operation in those patients in whom a diagnosis of nontoxic nodular goiter was made. However, some were referred to surgery at their own request and some were advised to have thyroidectomy because of cosmetic reasons or because of pressure effects. Certain patients were admitted directly to the surgery department. There were available for study 181 cases of patients with nontoxic nodular goiter in whom operation was not done and 171 in whom surgery was performed. In studying these case histories the symptoms found were nervousness or irritability, palpitation, tachycardia, shortness of breath, and weight loss. It was felt that it would be of interest to do follow-up studies on these patients and ascertain if those in whom partial thyroidectomy was done were relieved of these symptoms, and also to see whether those not operated upon had continued to have symptoms. This was done by questionnaires, therefore the results indicate the way the patient felt about the symptoms and are not a clinician's evaluation of the symptoms.

In all, 374 questionnaires were sent out, 235 were returned. The results are tabulated in Table I.

The average age of patients in the group not operated upon was 45.3 years. The average of those operated upon was also 45.3. In the patients operated upon and likewise in those not operated upon, 93 per cent were women.

**Nervousness and Irritability.**—Nervousness or irritability was the most frequent symptom and was manifested by 83 per cent of the patients in the group not operated upon on admission and 95 per cent of those operated upon. At the time of the follow-up, 71 per cent of those not operated upon still complained of this symptom while 79 per cent of those operated upon were relieved.

TABLE I

	QUESTIONNAIRES SENT		QUESTIONNAIRES RETURNED	
	NUMBER OF CASES	PER CENT	NUMBER OF CASES	PER CENT
All patients	374	100	235	63
Nonoperated	181	48	91	50
Operated	171	46	110	64
Returned by postoffice*	22	6		

\*Not included in either group operated upon or not operated upon. Effects to per cent returned of questionnaires sent out to this group.

TABLE II. SYMPTOMS ON ADMISSION AND ON FOLLOW UP

	ON ADMISSION					ON FOLLOW-UP					
	YES	NO		I		YES	NO		I		
	PER CENT	NUMBER OF PATIENTS	PER CENT	NUMBER OF PATIENTS	PER CENT	PER CENT	NUMBER OF PATIENTS	PER CENT	NUMBER OF PATIENTS	PER CENT	NUMBER OF PATIENTS
<i>Nonoperated</i>											
Nervousness or irritability	81	74	17	15	0	71	63	27	21	2	2
Palpitation or tachycardia	91	74	16	14	0	65	57	73	29	2	2
Shortness of breath	73	64	27	24	0	59	52	34	33	3	3
Weight loss	48	42	52	44	0	29	26	71	63		
<i>Operated</i>											
Nervousness or irritability	95	105	5	6	0	16	17	79	83	5	6
Palpitation or tachycardia	85	97	15	17	0	21	21	73	72	6	6
Shortness of breath	96	108	4	4	0	13	20	80	89	2	2
Weight	54	59	Loss		47	0	74	Gain since operation		25	1
			43					82			

\* represents patients who did not know how to answer the particular question

*Palpitation or Tachycardia*—Palpitation or tachycardia was present in 84 per cent of the group not operated upon and in 85 per cent of those operated upon on admission. Of those not operated upon 65 per cent reported that they still had pounding of the heart, while in those operated upon, 73 per cent were completely relieved of this symptom.

*Shortness of Breath*—In the group not operated upon, shortness of breath was noted in 73 per cent of the patients on admission and in those operated upon, in 96 per cent. Of those operated upon, 80 per cent were relieved while 59 per cent of those not operated upon still reported shortness of breath.

*Weight Loss*—Loss of weight was a less frequent symptom. Of the patients not operated upon, 48 per cent reported weight loss on admission and 29 per cent reported continued weight loss at the time of the follow-up. Of those operated upon, 54 per cent reported weight loss before the operation and 82 per cent reported that they had gained weight since the operation.

*Patients' Evaluation of Therapy*—In the group not operated upon, 8 per cent of the patients reported that they had improved, 11 per cent had progression of the symptoms, and 68 per cent reported that their condition was essentially unchanged, 13 per cent were equivocal. Of the patients operated upon, 59 per cent were improved, 9 per cent were worse, and 30 per cent were unchanged; 2 per cent were equivocal.

#### DISCUSSION

There are obvious objections to conclusions that are reached by a questionnaire study of this type. Nevertheless, they do show trends. Our results would

tend to bear out those who contend that the nodular goiter usually referred to as nontoxic is often associated with symptoms of nervousness and irritability, palpitation, tachycardia, and weight loss. These symptoms are present when the basal metabolic rate is within normal limits. On the basis of this study we feel that surgery is indicated in this group of patients and will result in the relief of symptoms present in patients with nontoxic nodular goiters in a significant percentage of cases.

# SUMMARY

1. Members of the medical and surgical departments in a series of medical schools were contacted relative to policies of management of patients having nontoxic nodular goiters. Replies were summarized.
2. For this study, 374 questionnaires were sent out to patients previously seen at the University of Iowa Hospitals who had been diagnosed as having nontoxic nodular goiters. Two types of questionnaires were used, one type going to those who had not been operated upon and a second type going to those who had been operated upon.
3. At the time of their admission about three-fourths of all these patients with so-called nontoxic nodular goiters suffered from symptoms often associated with hyperthyroidism in spite of normal basal metabolic rates.
4. Thyroidectomy resulted in regression of these symptoms in a large percentage of cases, whereas little change was noted in the group of patients who were not operated upon, after a period of from one to five years.
5. In one to five years after their discharge, 59 per cent of the group of patients who had operation were improved while 8 per cent of those not operated upon were improved.

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## GASTRIC RESECTION FOR PEPTIC ULCER

### A STUDY OF 221 CONSECUTIVE CASES

R. N. BARTFELS, M.D., AND J. W. DULIN, M.D., IOWA CITY, IOWA

(From the Department of General Surgery, University Hospitals)

FIVE years ago we reviewed our first experiences with gastric resection for peptic ulcer. That report<sup>1</sup> covered fifty consecutive gastric resections performed between 1927 and 1940 inclusive. From that study three significant facts were apparent to us: (1) our postoperative mortality was too high (28 per cent), (2) our indications for resection were too limited, and (3) our recurrent ulcer rate was too great (14.7 per cent). From the clinical and experimental evidence present in the literature, particularly the work of Wangensteen<sup>2</sup> in this country, it was apparent that we could lower the mortality, widen our indications for resection, and anticipate a lower rate of recurrent ulcer. One hundred consecutive gastric resections for benign ulcer, during the years 1941 to 1943, inclusive, furnish the material for a comparative study. Sufficient time has elapsed to allow an evaluation of the treatment of these cases and to determine to what degree we have attained the previously mentioned objectives.

*Sex and Age.*—There were eighty-eight men and twelve women in this series. The average age was 49.78 years, the majority of patients (57 per cent) being over 50 years of age. The proportionate number in each age group is shown in Table I.

*Symptoms.*—The duration of symptoms varied from three months to thirty years, the average being eleven and one-half years. Pain, indigestion, vomiting, and bleeding were the principal symptoms. The frequency of occurrence of these is seen in Table II. Most of the patients had multiple symptoms. Of particular interest were the number who had bleeding and the large number who were unable to work. The symptom of bleeding varied from occasional tarry stools or coffee ground emesis to massive hemorrhage-producing shock. This is a larger incidence of bleeding than is usually reported. In Rienhoff's<sup>3</sup> series hemorrhage as a symptom occurred in 42 per cent of 260 patients subjected to resection for chronic duodenal ulcer. McKittrick, Moore, and Warren<sup>4</sup> reported a history of bleeding in 30.8 per cent of thirty-nine patients who had a two-stage gastrectomy for duodenal ulcer. The degree of invalidism occurring with chronic peptic ulcer and its complications is often not appreciated by the physician. Table II shows that, of eighty patients on whom the information was available, sixty, or 86.2 per cent, were totally unable to work. Another four patients, or 5 per cent, were able to work only part time.

*Previous Treatment.*—A summary of the previous treatment is shown in Table III. Of the 100 patients, fifty-seven had been treated for their peptic ulcer by the Department of Medicine at the University Hospitals and thirty-six

TABLE I. AGE

AGE GROUP	NUMBER OF PATIENTS
20 to 29	9
30 to 39	16
40 to 49	18
50 to 59	15
60 to 69	18
70 to 79	4
Total	100

TABLE II SYMPTOMS

	PER CENT
Pain	93
Indigestion	91
Vomiting	77
Bleeding	64
Weight loss	80
Able to work	
No	86
Part time	5
Full time	9

medically by their local physician. Thus, 93 per cent had been given a trial of conservative therapy before resorting to gastric resection. It is not our intention to define what actually constitutes adequate medical therapy. Based on findings at operation, however, it has been our observation that symptoms of long duration, or frequent recurrence of symptoms, are associated with irreversible pathologic changes which no amount of medical therapy could benefit. We have performed emergency gastric resections for a massive hemorrhage or a free perforation upon patients who were receiving intensive medical therapy. Previous surgical treatment directed at the complications of peptic ulcer had been carried out on thirty of the 100 patients. Many of these operations were performed in our clinic. Table III shows that several of the patients had had more than one operation prior to resection. Twenty-two patients had had a closure of a free perforation, and three of these twenty-two had had a second free perforation.

*Primary Indication for Resection*—The primary indication for resection is shown in Table IV. Only the main indication is given, although many had more than one indication such as pain plus bleeding or pain plus obstruction. In the opinion of this clinic, the patient with ulcer who can be well controlled on medical therapy and carry on full-time work is not a candidate for gastric resection.

TABLE III PREVIOUS TREATMENT

Medical, 93	
University Hospital	
Local physician	
Surgical, 30	57
Closure perforated ulcer	36
Closure two perforations	
Gastroenterostomy	25
Excision of ulcer	3
Tearing down gastroenterostomy	8
Pyloroplasty	4
	1
	1

TABLE IV. PRIMARY INDICATION FOR RESECTION

	PER CENT
Pain	39
Obstruction	26
Bleeding	19
Gastric ulcer	7
Wrong diagnosis	7
Free perforation	1
Gastrojejunochole fistula	1

It is the uncontrolled patient with the complications of intractable pain, obstruction, hemorrhage, or perforation whom we consider for radical resection. Pain was the most common indication for resection, followed closely by obstruction. Bleeding was the reason for resection in 19 per cent of the patients. In eight of these hemorrhage was massive in character and resection was performed as an emergency. In nine patients recent severe hemorrhage had occurred, but no active bleeding was present at the time the operation was performed. In two other patients a marginal ulcer following gastrojejunostomy was the cause of the bleeding. A gastric ulcer which failed to heal under strict medical treatment was an indication for resection in seven patients. Progress in these patients was carefully followed by roentgenographic and gastroscopic examinations. We believe that gastric ulcers should be considered malignant until proved otherwise.

Seven per cent of the patients had an erroneous preoperative diagnosis. The diagnoses had been carcinoma of the stomach in three, cholelithiasis in three, and epigastric hernia in one. An emergency gastric resection was done in one instance for a free perforation of an anterior duodenal ulcer which occurred while the patient was on intensive conservative therapy. A gastrojejunochole fistula was the indication for resection in one instance.

*Location of Pathology.*—The location of the pathology is shown in Table V. In ten patients multiple ulcers were present either in the duodenum or stomach or both. A walled-off perforated gastric, duodenal, or jejunal ulcer was present in 59 per cent of the patients. A free perforation was present in one. An active ulcer without local perforation was present in 20 per cent. The remaining 20 per cent showed local stenosis, scarring, and distortion. Of the twenty-six patients resected primarily for obstruction, fifteen had a localized perforated ulcer.

TABLE V. LOCATION OF PATHOLOGY

	Total
Duodenal	7
Multiple, 6	
Gastric	21
Multiple, 1	
Gastric and duodenal	3
Marginal (jejunal)	5
Gastrojejunochole (fistula)	1

*Gastric Acidity Studies.*—In these 100 gastric resections a definite effort was made to produce postoperative achlorhydria, as determined by gastric analysis after histamine stimulation. For these studies fasting specimens were drawn and histamine phosphate  $\frac{1}{44}$  gr. (equaling essentially 0.5 mg. of histamine base)

was administered hypodermically. Samples were then drawn at intervals of fifteen, thirty, forty-five, and sixty minutes after injection. The free hydrochloric acid was determined by titration against a decinormal solution of sodium hydroxide using Töpfer's indicator. A comparison of the average free hydrochloric acid present preoperatively with the average free hydrochloric acid present during the immediate postoperative period and at follow-up examinations was made. The average determinations are shown in Fig. 1. There was essentially no difference in the amount of free acid present in the postoperative period and that present on follow-up examination one year later. The fact that the average determinations after operation show a minimal amount instead of an absence of free acid can be accounted for by an occasional patient who had a

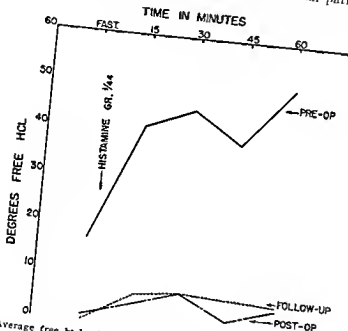


Fig. 1—Average free hydrochloric acid preoperative postoperative and follow up

moderate amount of free hydrochloric acid present after operation. A few individuals had achlorhydria in the postoperative period but showed some free acid on subsequent follow up, while the reverse was true in a few others. There is no explanation of this change-over in the small per cent of patients where it occurred. Obviously the complete achlorhydria is a relative achlorhydria. There is a small amount of free hydrochloric acid produced by the stomach remnant but this is neutralized by pancreatic juice and bile.

*Relation of Amount of Stomach Resected to Reduction of Free Hydrochloric Acid*—Opinions differ among surgeons as to whether radical resection of the stomach is necessary in the surgical treatment of peptic ulcer. Wangenstein favors a three-quarters resection and has presented much clinical and experimental evidence to support his views. He thinks it is best to obtain an achlor-



hydria in all patients. Rienhoff<sup>3</sup> and Heuer and associates,<sup>4</sup> among others, believe that a less radical resection is satisfactory and carries a lower operative mortality. Heuer and associates<sup>4</sup> have stated that achlorhydria postoperatively is not necessarily related to a good result.

Because of these divergent opinions an attempt was made to determine in these 100 patients the relation of the amount of stomach removed to the reduction in acidity and to the clinical end result. In 80 per cent of the patients, two-thirds or more of the stomach was resected. The remaining 20 per cent, who had conservative resections, were operated early in the series when we were formulating our opinions. Of the eighty cases, nine had a four-fifths resection, twenty-eight a three-quarters resection, and forty-three a two-thirds resection. The portion of stomach removed was not weighed or measured, the amount removed being estimated by the surgeon. In Table VI are shown the results of gastric analyses performed on follow-up examination of the patients who had radical resections. Fifty-six of the eighty patients had gastric analyses available for comparison, and of these forty-one, or 73 per cent, had achlorhydria after histamine stimulation. The average age of the groups of patients shown in Table VI indicates that an attempt was made to be more radical in the younger individual. It is of interest that there was a greater percentage of patients with achlorhydria among those who had a two-thirds resection than in those who had a three-quarters resection. The explanation of this finding is not apparent. The recent studies of Wangersteen<sup>5</sup> in regard to a short afferent loop may be of importance here. Unfortunately the length of the afferent loop was not measured. We favor a short afferent loop because we think it gives a better functioning anastomosis. It is possible to use a shorter afferent loop after two-thirds resection than after a more radical resection. If one assumes that a shorter afferent limb was utilized after two-thirds resection than after three-quarters resection then possibly the shorter proximal limb of the anastomosis becomes more important in producing a relative achlorhydria than the difference between removing two thirds or three-quarters of the stomach. We are making an investigation of this problem at the present time.

TABLE VI. RELATIONSHIP OF AMOUNT OF STOMACH RESECTED TO REDUCTION OF FREE HCL.

AMOUNT RESECTED	NUMBER OF PATIENTS	NUMBER AVAILABLE FOR STUDY	AVERAGE FOLLOW-UP GASTRIC ANALYSIS (DIGESTIVE FIVE HCL)				NUMBER ACHLOR- HYDRIC	PER CENT ACHLOR- HYDRIC	AVERAGE AGE (YEARS)
			15 FAST	30 MIN.	45 MIN.	60 MIN.			
Four fifths	9	5	0	0	5	0	4	80	41.8
Three fourths	28	24	1	7	9	8	14	66.7	46.9
Two thirds	43	30	0	5	4	1	23	76.7	50.0

*Method of Operation.*—All gastrojejunal anastomoses were of the termino-lateral, oralis totalis type. Ninety-nine were retrocolic and one antecolic. An associated enteroenterostomy was performed in five instances, one in the antecolic and one in a classical retrocolic anastomosis. The other three enteroenterostomies were of the en-y type, performed after jejunal resection for a marginal ulcer. We believe that associated enteroenterostomy is unnecessary.

and may predispose to recurrent ulcer. Resection with pyloric exclusion and removal of the antral mucosa was performed in four patients. This reflects our opinion that so called "irremovable" duodenal ulcers are not common. In most instances of perforating posterior duodenal ulcers we remove the ulcer and dissect free sufficient posterior duodenal wall for adequate closure. The closure of the pyloric stump after pyloric exclusion has not been satisfactory in our experience. In none of our cases have we felt it necessary to place a T tube in the common bile duct for identification of this structure, as advised by Lahey.<sup>7</sup> Recently we have closed the duodenal stump in two patients by the method described by Wangensteen<sup>8</sup> and Nissen.<sup>9</sup> By this technique the anterior duodenal wall is inverted into the posterior duodenal wall without mobilizing the latter. It obviates possible damage to the retroduodenal structures.

*Nonfatal Postoperative Complications*.—Thirty-one per cent of the patients had major, nonfatal postoperative complications. These are listed in Table VII. Nine, or 29 per cent, of the complications were pulmonary. Five patients had primary wound infections. It was necessary that one patient be re-operated because of an obstructed anastomosis, an anterior gastrojejunostomy and enteroenterostomy was performed twenty days after resection. In three patients there was delayed function of the anastomosis; however, all of these cleared up with gastric suction. One patient developed symptoms and findings of incomplete obstruction of the small intestine which responded to conservative treatment. In two patients the lesser pancreatic duct was divided at operation. In one of these cases there was a marginal ulcer and an associated posterior duodenal ulcer perforated into the pancreas. In the other there was a perforated lesser curvature pyloric ulcer with a walled-off abscess cavity containing 200 cc of pus and gastric contents. A temporary pancreatic fistula developed in both instances but closed spontaneously. Temporary jaundice was the main complication in two patients. In these the icterus was due to intraperitoneal sulfanilamide implanted at operation. No jaundice occurred in fifty-nine other patients in whom intraperitoneal sulfonamides were used. Wound separation without evisceration, not requiring secondary closure, occurred in two patients. Another patient had an evisceration closed by secondary suture. An intra-

TABLE VII MAJOR POSTOPERATIVE COMPLICATIONS  
(NONFATAL)

Pneumonia	7
Atelectasis	2
Wound infection	5
Delayed function of anastomosis	3
Obstructed anastomosis (reoperated)	1
Incomplete intestinal obstruction	1
Laryngeal Edema (tracheotomy)	1
Temporary pancreatic fistula	2
Jaundice	2
Wound separation (without evisceration)	2
Evisceration (secondary closure)	1
Intra abdominal abscess (drainage)	2
Ascites (reoperated)	1
Bleeding from gastrointestinal tract	1
Total	31

abdominal abscess, requiring drainage, occurred in two patients. One patient developed marked ascites requiring repeated paracentesis. On reoperation aseptic necrosis of a portion of the great omentum was found. Bleeding from the gastrointestinal tract continued for ten days after resection in one patient. Laryngeal edema, a complication of the intratracheal anesthesia, occurred in one patient and required that a tracheotomy be performed.

**Mortality.**—There were eight deaths. Five of these occurred in the group of twenty patients having less than two thirds of the stomach removed, while the other three deaths were in the group of eighty patients who had two-thirds or more of the stomach removed. From this it would appear that the magnitude of stomach resection per se does not increase the mortality rate. In four of the eight patients the indication for resection was a serious complication of ulcer or of the previous inadequate surgical treatment. Two of these underwent emergency resection for massive hemorrhage, one was resected for a marginal ulcer, and one for a gastrojejunocolic fistula, both of which followed gastroenterostomy.

The other four patients who died had elective resections for pain or obstruction. In two, cardiac failure was the cause of death, while peritonitis was responsible for the other two deaths.

The average age of the eight patients who died was 60.2 years in contrast to the average age of 49.78 years of the entire series. We do not think that the elderly patients should be denied the benefit of gastric resection because of the age factor alone. Reports of the eight postoperative deaths follow.

#### CASE REPORTS

**CASE 30.**—J. B. (hospital No. 39 131241), a 54 year old white man, had a gastrojejunostomy performed in this hospital Feb. 21, 1940, for duodenal ulcer. He developed recurrence of pain and bleeding. He had a severe case of asthma and had a marked anemia. The latter required seven blood transfusions before operation. Indication for resection was marginal ulcer with pain and bleeding. Operation was done on June 24, 1942. A marginal ulcer, 1 cm. in diameter, was found in the jejunum opposite the stoma. Three fifths of the stomach was removed. A postcolic, terminolateral, oralis totalis gastrojejunostomy re-established the continuity of the gastrointestinal tract. A resection of the jejunum containing the ulcer was considered but the ileum was abandoned and the jejunal opening closed, the new jejunal stoma being made distal to the site of closure. After resection the patient developed atelectasis. He developed a wound separation and this was followed by a jejunal fistula. On Oct. 1, 1942, he was reoperated and the fistula containing segment of jejunum (in the afferent limb) was resected and an end-to-end anastomosis performed. This jejunal anastomosis broke down. He became weaker and died on Oct. 19, 1942, eighteen days after jejunal resection and 119 days after gastric resection. Autopsy revealed jejunal fistula and left subphrenic abscess.

**Comment.**—It would have been better to have resected the involved jejunum at the time of gastric resection.

**CASE 47.**—G. O'N. (hospital No. 42 13166) was a 69 year old white man. Fifteen years before admission he was treated medically for "ulcers" and recovered. He developed recurrence of pain six weeks before admission and had tarry stools and severe episodes of hematemesis, which required hospitalization the week before entrance to our service. On admission the hematemesis had ceased but he had tarry stools. Blood studies revealed a

hemoglobin of 3.8 Gm, and the red blood cell count was 1,900,000 per cubic millimeter. The patient was given nothing by mouth, morphine  $\frac{1}{4}$  gr by hypodermic, and three 500 c.c. blood transfusions. Because the hematocrit had subsided and because of the severe anemia, we decided to try conservative treatment to build him up for elective resection. However, the following day, Nov 15, 1942, he had a massive hematemesis, accompanied by shock. An emergency operation revealed a perforated posterior duodenal ulcer with an actively bleeding artery in the ulcer crater. The bleeding vessel was controlled by transfixion suture. The ulcer bearing area of the duodenum and 50 per cent of the stomach were removed. Gastrointestinal tract continuity was reestablished by a postcolic, terminolateral, oralis totalis gastrojejunostomy. Postoperatively the patient was given 2,500 c.c. of blood. On Nov. 18, 1942, he eviscerated and secondary closure was performed. He died on the operating table. Autopsy revealed localized peritonitis, wound infection, pleural effusion, and pulmonary edema. The duodenal stump closure and gastrojejunostomy suture lines were intact.

**Comment**—The ideal time for resection was when he had his first bleeding. A patient who has lost large amounts of blood over a period of time is a poor operative risk even though supported by many transfusions.

**CASE 52**—C C (hospital No 42 13156), a 37 year old white man, had had symptoms of ulcer and vomiting for twenty years. Stools had been tarry for one week. He had chronic heart disease and was receiving digitalis. Indications for resection were continued pain and a large gastric ulcer not controlled by conservative treatment. Operation was done on Nov. 20, 1942. A posterior gastric ulcer, perforated into the pancreas, was found. The proximal duodenum and three fifths of the stomach were removed. Continuity of the gastrointestinal tract was reestablished by a postcolic, terminolateral, oralis totalis gastrojejunostomy. Twenty four hours after operation the patient developed clinical signs of cardiac failure. He failed to respond to treatment and died on the sixth postoperative day. Clinical cause of death was cardiac failure. Autopsy was not granted.

**Comment**—This patient had continuous severe pain which could not be relieved by the most strict conservative measures. For this reason gastric resection was indicated even though he had severe heart disease.

**CASE 63**—M I (hospital No 42 14394), a 69 year old white man, had had symptoms of ulcer, chiefly pain with occasional episodes of vomiting, for twenty eight years. Indication for resection was increasing pain in spite of conservative treatment on the medical service. Operation was done on Feb 5, 1943. Exploration revealed a very active duodenal ulcer along the superior border, with stenosis distal to the ulcer, considerable scarring, and inflammation in the periduodenal tissues. Resection of one half of the stomach, with exclusion of the pylorus and removal of the antral mucosa, was performed. It was felt that removal of the involved duodenum might result in damage to the common bile duct. Twenty four hours after operation he developed fever and right upper abdominal pain. On Feb 12, 1943, a right subhepatic abscess was drained. The patient died on Feb 13, 1943. Autopsy revealed generalized peritonitis due to necrosis and leakage of pyloric stump, subhepatic and subphrenic abscesses, unilateral empyema thoracis, and bronchopneumonia.

**Comment**—In difficult posterior duodenal ulcers we have usually mobilized the duodenum for closure. We have preferred this method because of the difficulty in obtaining a secure closure of the pyloric stump after exclusion and removal of the antral mucosa. However, recent studies and improvements in our technique of pyloric stump closure lead us to believe that this method may be used without undue danger.

**CASE 70**—M. T. (hospital No 40 8113), a 54 year old white man, had had symptoms of ulcer for thirty years. He had had medical treatment at another clinic, by several local

physicians, and by the medical department of this hospital. He was first admitted to the surgical service in 1940, at which time an acute perforation of a duodenal ulcer was closed. Persistent postoperative vomiting ensued and a posterior gastrojejunostomy was performed. Ten months before the last admission to the surgical service the patient began to have hematemesis and tarry stools. Four months before admission he developed diarrhea and foul breath and began to have bowel movements immediately after eating. A barium enema revealed a gastrojejunocolic fistula. A double barreled colostomy, utilizing the right transverse colon, was performed on Feb. 19, 1943, as a preliminary measure to resection. The second stage was delayed until April 9, 1943, because he developed lobar pneumonia. At the second operation the jejunum distal to the old gastrojejunostomy was found adherent to the colon. A moderately large fistula was present between the colon and jejunum just distal to the anastomosis. There was a posterior duodenal ulcer perforated into the pancreas. The old gastrojejunostomy was disengaged and the colonic fistula closed. The ulcer-bearing area of the duodenum and three quarters of the stomach were removed. The jejunal stoma and fistula were converted into one opening, which allowed it to be used for the new jejunal stoma. Continuity of the gastrointestinal tract was then reestablished by a postcolic, terminolateral, oralis totalis gastrojejunal anastomosis. Postoperatively the patient developed fever, jaundice and abdominal pain, tenderness, and rigidity. He became weaker and died on April 17, 1943. Autopsy revealed generalized bile peritonitis due to a defect and traumatic stricture of the common bile duct, atelectasis, and left perinephric abscess.

*Comment.*—This case is the only proved one of operative injury to the common bile duct.

CASE 74.—P. H. (hospital No. 434045), a 68 year old white man, had had symptoms of ulcer for forty years. He also had severe pain, occasionally requiring morphine, vomiting, and hematemesis, for three weeks before admission. He had been in a local hospital during this three week period. On admission to our service, April 20, 1943, blood studies revealed the hemoglobin to be 43 Gm., and the red blood cells were 1,590,000 per cubic millimeter. A gastric series taken the day after admission revealed pyloric obstruction, probably due to a duodenal ulcer, with 90 per cent gastric retention. On April 22, 1943, the stomach was aspirated and 1,200 c.c. of coffee ground material obtained. On April 23, 1943, he had a massive hematemesis accompanied by shock, the hemoglobin was less than 7 Gm., and the erythrocytes were 1,590,000 per cubic millimeter. An emergency gastric resection seemed indicated because of recurrent massive bleeding. The patient was given a total of 3,000 c.c. of blood before and during the operation. On exploration anterior and posterior kissing duodenal ulcers were found. The anterior ulcer was of the perforating type, and the posterior one had perforated through the duodenal wall into the pancreas. A vigorously bleeding artery was present in the ulcer crater and was controlled by transfixion sutures. A 900 c.c. blood clot was removed from the stomach. There was marked scarring and stenosis of the duodenum distal to the ulcers. The involved duodenum and one half of the stomach were removed. Continuity of the gastrointestinal tract was reestablished by a postcolic, terminolateral, oralis totalis gastrojejunostomy. At the beginning of the operation the blood pressure was 60 mm. Hg systolic and 40 mm. Hg diastolic. At the conclusion of the operation the blood pressure was 90 mm. Hg systolic and 50 mm. Hg diastolic. In the immediate postoperative period he received two additional 500 c.c. blood transfusions. On the second postoperative day he became jaundiced, the van den Bergh reaction was 200 direct. Five additional 500 c.c. blood transfusions were given during the postoperative period. The course was febrile, the patient became weaker, and death occurred on May 1, 1943, on the ninth postoperative day. Autopsy revealed generalized peritonitis due to separation of gastrojejunal suture line, cellulitis of abdominal wall, right bronchopneumonia, left lower lobe atelectasis, and bilateral pleurisy and pericarditis.

*Comment.*—Poor healing related to the great blood loss was responsible for the separation of the suture line and fatal peritonitis. The blood trans-

fusion service quite definitely determined that the jaundice was due to the transfusion of excessive amounts of free hemoglobin. This case is similar to Case 47, in that massive bleeding occurred while the patient was being prepared for elective resection. This type of patient is a notoriously poor operative risk. Earlier operative intervention, before succeeding exsanguinating hemorrhages occur, will give a lower operative mortality.

CASE 79—C. S. (hospital No. 43 5356), a 37 year old white man, had had symptoms of ulcer, chiefly pain and vomiting, for one year. Gastric series showed a stenosing duodenal ulcer with 100 per cent retention in five hours. Indication for resection was obstruction and pain which was unrelieved by conservative treatment on the medical service. Operation was done on June 16, 1941. At operation multiple duodenal ulcers, two anterior and one posterior, with marked duodenal stenosis were found. The involved duodenum and two thirds of the stomach were removed. Gastrojejunostomy anastomosis was reestablished by a postcolic, terminalateral, orals totals gastrotomy. On the fourth postoperative day the patient began to develop noticeable jaundice. On June 30, 1941, a left subhepatic abscess, containing 900 cc of fluid that appeared to be bile, was drained. No organisms grew out of this fluid on culture. On July 4, 1941, 8 liters of bile stained fluid were removed from the abdomen by paracentesis. On July 8, 1941, the right subphrenic and subhepatic areas were explored, by anterior approach, and 4,000 cc of bile stained fluid removed. A fibrin covered mass in the gall bladder area was aspirated and 6 cc of pus obtained. This latter material yielded *Escherichia coli* on culture. The patient became weaker and died on July 19, 1941. Clinical cause of death was bile peritonitis, due to possible rupture of the gall bladder, common bile duct, or other extrahepatic ducts, and possible suppurative pancreatitis. Autopsy was not granted.

Comment—This case definitely did not appear like one with a blowout of the duodenal stump. This we believe represents our second operative injury to the common duct which caused a blowout in the extrahepatic system.

CASE 97—J. E. (hospital No. 47 12091), a 72 year old white man, had had symptoms of ulcer, chiefly pain and vomiting, for two years. A gastric series showed what appeared to be a duodenal ulcer with 90 per cent retention in six hours. Indication for resection was obstruction. Operated on Nov. 23, 1941. Exploration revealed a posterior pyloric ulcer perforated into the pancreas. The ulcer crater in the pancreas measured 4 cm. in diameter. There was a small abscess on the superior surface of the duodenum with marked duodenal stenosis. The involved duodenum and two thirds of the stomach were removed. Gastrojejunostomy anastomosis was reestablished by a postcolic, terminalateral, orals totals gastrotomy. Postoperatively the patient developed cardiac failure which failed to respond to treatment and died on Nov. 28, 1941. Autopsy revealed left sided cardiac hypertrophy and marked pulmonary emphysema.

Comment—Aged patients with poor cardiac reserve may be accepted for resection when the disease cannot be controlled by conservative measures.

# RESULTS

There were ninety-two patients available for follow-up studies. Fifty-nine, or 64.1 per cent, were followed by examination at the hospital or by letters to the patients. There were fifty-two in the former and seven in the latter group. Most of the remaining patients were followed indirectly by information obtained from the local physician. The results were classified in three groups: well, improved, or recurrent. To be classified as well a patient must have been free of all ulcer symptoms, eating well and working full time, or carrying on normal

physicians, and by the medical department of this hospital. He was first admitted to the surgical service in 1940, at which time an acute perforation of a duodenal ulcer was closed. Persistent postoperative vomiting ensued and a posterior gastrojejunostomy was performed. Ten months before the last admission to the surgical service the patient began to have hematemesis and tarry stools. Four months before admission he developed diarrhea and foul breath and began to have bowel movements immediately after eating. A barium esoma revealed a gastrojejunocolic fistula. A double barreled colostomy, utilizing the right transverse colon, was performed on Feb. 19, 1943, as a preliminary measure to resection. The second stage was delayed until April 9, 1943, because he developed lobar pneumonia. At the second operation the jejunum distal to the old gastrojejunostomy was found adherent to the colon. A moderately large fistula was present between the colon and jejunum just distal to the anastomosis. There was a posterior duodenal ulcer perforated into the pancreas. The old gastrojejunostomy was disengaged and the colonic fistula closed. The ulcer bearing area of the duodenum and three quarters of the stomach were removed. The jejunal stoma and fistula were converted into one opening, which allowed it to be used for the new jejunal stoma. Continuity of the gastrointestinal tract was then re-established by a postcolic, terminolateral, oralis totalis gastrojejunal anastomosis. Postoperatively the patient developed fever, jaundice and abdominal pain, tenderness, and rigidity. He became weaker and died on April 17, 1943. Autopsy revealed generalized bile peritonitis due to a defect and traumatic stricture of the common bile duct, atelectasis, and left nephritic abscess.

*Comment*—This case is the only proved one of operative injury to the common bile duct.

CASE 74—P. H. (hospital No. 434045), a 64 year old white man, had had symptoms of ulcer for forty years. He also had severe pain, occasionally requiring morphine, vomiting, and hematemesis, for three weeks before admission. He had been in a local hospital during this three week period. On admission to our service, April 20, 1943, blood studies revealed the hemoglobin to be 4.3 Gm., and the red blood cells were 1,590,000 per cubic millimeter. A gastric series taken the day after admission revealed pyloric obstruction, probably due to a duodenal ulcer, with 90 per cent gastric retention. On April 22, 1943, the stomach was aspirated and 1,700 cc of coffee ground material obtained. On April 23, 1943, he had a massive hematemesis accompanied by shock, the hemoglobin was less than 7 Gm., and the erythrocytes were 1,520,000 per cubic millimeter. An emergency gastric resection seemed indicated because of recurrent massive bleeding. The patient was given a total of 3,000 cc of blood before and during the operation. On exploration anterior and posterior living duodenal ulcers were found. The anterior ulcer was of the perforating type, and the posterior one had perforated through the duodenal wall into the pancreas. A vigorously bleeding artery was present in the ulcer crater and was controlled by trans-fixion sutures. A 900 cc. blood clot was removed from the stomach. There was marked scarring and stenosis of the duodenum distal to the ulcers. The involved duodenum and one half of the stomach were removed. Continuity of the gastrointestinal tract was re-established by a postcolic, terminolateral, oralis totalis gastrojejunostomy. At the beginning of the operation the blood pressure was 80 mm Hg systolic and 40 mm Hg diastolic. At the conclusion of the operation the blood pressure was 90 mm Hg systolic and 50 mm Hg diastolic. In the immediate postoperative period he received two additional 500 cc blood transfusions. On the second postoperative day he became jaundiced, the van den Bergh reaction was 200 direct. Five additional 500 cc. blood transfusions were given during the postoperative period. The course was febrile, the patient became weaker, and death occurred on May 1, 1943, on the ninth postoperative day. Autopsy revealed generalized peritonitis due to separation of gastrojejunal suture line, cellulitis of abdominal wall, right bronchopneumonia, left lower lobe atelectasis, and bilateral pleurisy and pericarditis.

*Comment*—Poor healing related to the great blood loss was responsible for the separation of the suture line and fatal peritonitis. The blood trans-

fusion service quite definitely determined that the jaundice was due to the transfusion of excessive amounts of free hemoglobin. This case is similar to Case 47, in that massive bleeding occurred while the patient was being prepared for elective resection. This type of patient is a notoriously poor operative risk. Earlier operative intervention, before succeeding exsanguinating hemorrhages occur, will give a lower operative mortality.

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**Comment**—This case definitely did not appear like one with a blowout of the duodenal stump. This we believe represents our second operative injury to the common duct which caused a blowout in the extrahepatic system.

CASE 87—J. E. (hospital No. 41 12091), a 72 year old white man, had had symptoms of ulcer, chiefly pain and vomiting, for two years. A gastric series showed what appeared to be a duodenal ulcer with 90 per cent retention in six hours. Indication for resection was obstruction. Operated on Nov. 23, 1943. Exploration revealed a posterior pyloric ulcer perforated into the pancreas. The ulcer crater in the pancreas measured 4 cm. in diameter. There was a small abscess on the superior surface of the duodenum with marked duodenal stenosis. The involved duodenum and two thirds of the stomach were removed. Gastrointestinal tract continuity was reestablished by a postcolic, terminolateral, orals totalis gastrojejunostomy. Postoperatively the patient developed cardiac failure which failed to respond to treatment and died on Nov. 28, 1943. Autopsy revealed left sided cardiac hypertrophy and marked pulmonary emphysema.

**Comment**—Aged patients with poor cardiac reserve may be accepted for resection when the disease cannot be controlled by conservative measures.

#### RESULTS

There were ninety-two patients available for follow-up studies. Fifty-nine, or 64.1 per cent, were followed by examination at the hospital or by letters to the patients. There were fifty-two in the former and seven in the latter group. Most of the remaining patients were followed indirectly by information obtained from the local physician. The results were classified in three groups: well, improved, or recurrent. To be classified as well a patient must have been free of all ulcer symptoms, eating well and working full time, or carrying on normal



daily life. The improved classification signified that the patient was free of pain and all other ulcer complaints, but other symptoms, such as weakness or poor appetite, were present. Any patient who had recurrent symptoms after resection, such as pain, hemorrhage, distress, or vomiting, was classified as having recurrent ulcer, regardless of whether it could be demonstrated by roentgenographic examination. A stringent classification of results must be adopted if we are to evaluate properly the place of gastric resection in the treatment of peptic ulcer.

The fifty-nine patients who were followed directly were classified as follows: well, fifty-one, or 86.4+ per cent; improved, four, or 6.7+ per cent; recurrent, four, or 6.7+ per cent. There was no evidence of recurrent ulcer in any of the thirty-three patients followed indirectly. Reports from the local physician usually stated that the patient was well and working and did not care to return for a checkup examination. Due to the method of handling the care of patients in this state clinic, most of the patients treated by us who later develop complications are returned to us for further care.

Studies of the possible cause or causes of recurrence in four patients are of interest. Pertinent information regarding these cases is shown in Table VIII and in the case reports. In two of the patients, Cases 14 and 68, we feel that removal of an inadequate amount of stomach was the cause of the recurrence. In the other two, Cases 50 and 75, the answer is not so apparent. Both of these had three-quarters resections which would appear to be adequate to forestall the development of a recurrent ulcer. However, both of these patients were resected because of marginal ulcer, and resection of the portion of the jejunum containing the ulcer was required. Gastrointestinal tract continuity was then re-established by closing the end of the distal jejunal segment and anastomosing

TABLE VIII. RECURRENCES

CASE NO. PATIENT	AGE	INDICATION FOR RESECTION	AMOUNT OF STOMACH RESECTED	TYPE OF ANAS- TOMOSIS	FOLLOW UP GASTRIC ANALYSIS				COMMENTS
					FAST	15	30	60	
14, C. V.	54	Recent severe bleeding	$\frac{2}{3}$	Polya	-	-			Marginal ulcer, died two years and eight months after resec- tion with gastro- jejunocolic fistula
50, R. McC.	60	Marginal ulcer	$\frac{3}{4}$	Polya resection jejunum en y	0	41	64	79	Symptoms of mar- ginal ulcer
68, L. M.	56	Recent severe bleeding	$\frac{1}{2}$	Polya	0	0	27	34	Marginal ulcer; un- der conservative treatment twenty six months after re- section
75, E. T.	45	Marginal ulcer	$\frac{3}{4}$	Polya resection jejunum en y	10	41	55	73	Died of hemorrhage and local perfora- tion of marginal ulcer twenty five months after resec- tion
Average					3	23	49	48	

it to the stomach by the terminolateral, oralis totalis method. The end of the proximal jejunal segment was then anastomosed, end to side, to the distal jejunal segment distal to the gastrojejunal anastomosis. On the basis of Wangenstein's recent report regarding the function of the short afferent loop, these recurrences may be blamed on the en-y type of jejunojejunostomy. It would appear essentially impossible for the free hydrochloric acid from the remaining gastric pouch to reach the duodenal mucosa and thus stimulate the production of secretin. Furthermore, the buffering effect of the alkaline bile and pancreatic juice that is secreted is lost, since these juices by-pass the gastrojejunal anastomosis, leaving it exposed to the acid-peptic digestive juice. One other patient, resected for a marginal ulcer, had a two-thirds gastric resection with resection of the jejunum and this same type of en-y jejunojejunostomy.

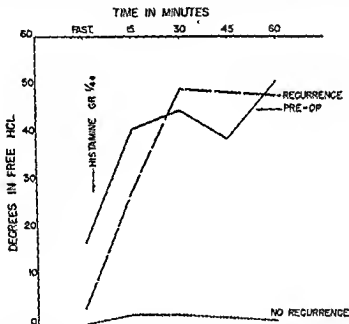


Fig. 2.—Comparison of the free hydrochloric acid in patients with recurrent ulcer and in patients without recurrence. For clarity the average preoperative acid curve is included.

Follow-up determinations of the amount of free hydrochloric acid, after histamine stimulation, are available in three of the four patients with recurrent ulcer. Case 14 had a personal checkup but unfortunately gastric analysis was not done. Case 50 was examined in our clinic five months after operation and a gastric analysis was done. He was well at that time, but fifteen months later his local physician reported him to be under treatment for a marginal ulcer. In Fig. 2 is shown the preoperative free hydrochloric acid curve compared with the free hydrochloric acid curves of the patients with recurrent ulcer and those with no recurrences. It is noted that the free acid curve of the patients with recurrent ulcer is as high, or higher, than the preoperative curve. This indicates that the acid values in recurrent ulcers are essentially the same as the values

obtained preoperatively when the original ulcer was present and that a relative achlorhydria is necessary to prevent recurrence.

A direct relationship between recurrent ulcer and conservative resection is evident in this series. In twenty patients who had less than a two-thirds resection, a recurrent ulcer developed in two of the fifteen survivors, a recurrence rate of 13.3 per cent. In eighty patients who had two-thirds or more of the stomach resected, recurrent ulcer developed in two of the seventy-seven survivors, a recurrence rate of 2.59 per cent.

During the same years, 1941 to 1943 inclusive, there were eleven patients treated for ulcer by gastroenterostomy. Nine of these were done in 1941, one in 1942, and one in 1943. Recurrent ulcer developed in three of the eleven patients, a recurrence rate of 27.3 per cent. Reports of the four patients with recurrent ulcer are as follows.

#### CASE REPORTS

**CASE 14**—C V. (hospital No 42531), a 54 year old white man, had had symptoms of ulcer, consisting of severe pain with nausea and vomiting, for three months. He had a massive hemorrhage six weeks before admission. On entrance he showed a severe anemia which required three blood transfusions before operation. Indications for resection were recent severe bleeding and continued pain. Operation was done on Jan 22, 1942. Exploration revealed anterior and posterior duodenal ulcers, the posterior one was perforated into the pancreas. The ulcer bearing area of the duodenum and two fifths of the stomach were removed. Gastrointestinal tract continuity was reestablished by a postcolic, terminolateral, oralis totalis gastroyejunostomy. The postoperative course was uneventful and the patient was discharged on the fifteenth postoperative day. He was readmitted to the hospital on Feb 13, 1943. He had had recurrence of severe ulcer pain, with vomiting, indigestion, weakness, and weight loss. Gastric series showed the anastomosis to be functioning well, there was no evidence of marginal ulcer. However, we felt that he did have a marginal ulcer despite negative roentgenographic findings. The patient was placed on medical management for a week and then discharged to the care of his home physician. He continued to have recurrent symptoms. In September, 1944, he entered another hospital with evidence of a gastrojejunochole fistula. While he was being prepared for surgery an ulcer was perforated and the patient died several days after an emergency exploration.

*Comment*—This recurrence was due to removal of an inadequate amount of stomach. A resection should have been performed in February, 1943, when we first diagnosed the marginal ulcer.

**CASE 50**—R McC. (hospital No 4213182), a 60 year old white man, had had symptoms of ulcer for sixteen years. He had a gastroenterostomy performed in this clinic in 1936. This was followed by recurrence of pain and five episodes of bleeding. Indication for resection was recent severe hemorrhage and marginal ulcer. Operation was done on Nov 18, 1942. Exploration revealed a jejunal ulcer opposite the stoma, which had perforated into the jejunal mesentery. A posterior duodenal ulcer, perforating into the pancreas, was also present. The ulcer bearing area of the duodenum, three fourths of the stomach, and a 6 inch segment of jejunum were resected. A postcolic, terminolateral, oralis totalis gastroyejunostomy and en y jejunojejunoctomy reestablished the continuity of the gastrointestinal tract. A complication of the operation was the inadvertent division of the lesser pancreatic duct. Postoperatively there was drainage of pancreatic juice from the abdominal wound but it subsided spontaneously. Gastric analysis after operation showed 38 and 52 degrees of free hydrochloric acid at intervals of thirty and sixty minutes, respectively, after histamine. The patient was discharged on the forty third postoperative day. He returned for examination five months

later. He had gained 20 pounds in weight. His strength was fair and he was working half time. He had no ulcer symptoms. Gastric analysis was done and the results are seen in Table VIII. Gastric series showed a normally functioning stoma without evidence of a marginal ulcer. Four months later a letter from the local physician reported that the patient had symptoms of a recurrent ulcer and was on medical management.

*Comment*—We think that the recurrent ulcer was due to the en-y type of enteroenterostomy carried out in conjunction with the gastrojejunostomy.

CASE 68.—L. M. (hospital No. 432198), a 56 year old white man had had symptoms of ulcer, essentially pain, in the spring and fall, for fifteen years. He had had four moderate to severe episodes of bleeding, the most recent occurring nine days before admission. Indication for resection was recent severe bleeding. Operation was done on April 1, 1943. A posterior duodenal ulcer, perforating into the pancreas, was found. The ulcer bearing area of the duodenum and one half of the stomach were removed. A postcolic, terminolateral, oralis totalis gastrojejunostomy was performed. The patient was discharged on the thirteenth postoperative day. He was readmitted to the hospital June 21, 1944. He complained of episodes of pain when he worked exceptionally hard and had had a small hematemesis a few days before. Gastric series showed a normally functioning anastomosis without evidence of a recurrent ulcer. Our clinical diagnosis was marginal ulcer. The patient was symptom free after two days of medical management. He was readmitted to the hospital June 20, 1945. He stated that he was able to work but had ulcer pain between meals. He had been taking a simple general diet divided in five small meals and had gained 20 pounds in weight since the previous admission. Gastric analysis was done and the results are seen in Table VIII. A gastric series showed a normally functioning anastomosis without evidence of a marginal ulcer. We again made a clinical diagnosis of marginal ulcer. The symptoms subsided after three days of hospitalization and medical treatment. The patient was advised to have another gastric resection, but he felt it wasn't necessary and returned home because he had "lots of work to do."

*Comment*.—In this case the removal of an insufficient amount of stomach is the cause of the recurrent ulcer. The patient should have a re-resection.

CASE 75.—E. T. (hospital No. 434308), a 45 year old white man had had symptoms of ulcer for twelve years. In January, 1932, a free perforation was closed at another hospital. In June, 1932, a gastroenterostomy was performed elsewhere. On Dec. 16, 1942, a second free perforation was closed at a local hospital. The patient's chief complaints, on admission to our service, were pain and vomiting. Indication for resection was pain and a marginal ulcer. Operation was done on May 6, 1943. The duodenum revealed marked scarring. There was a jejunal ulcer opposite the stoma. The involved portions of the proximal duodenum, jejunum, and three quarters of the stomach were resected. The continuity of the gastrointestinal tract was re-established by postcolic, terminolateral, oralis totalis gastrojejunostomy and en-y jejunojejunostomy. After operation a gastric analysis revealed the following free hydrochloric acid values: fasting, 37 degrees, fifteen minutes, 27 degrees, thirty minutes, 33 degrees; sixty minutes, 34 degrees. The patient had an uneventful course and was discharged on the fourteenth postoperative day. He returned in September, 1944, having gained 17 pounds in weight. He was eating five meals a day and was not restricting the diet as to type of food. His only complaint was a feeling of fullness immediately after meals. Gastric analysis was done and the results are seen in Table VIII. The patient was readmitted to the hospital June 14, 1945, because of pain, nausea, and vomiting of four months' duration. The pain had been severe for one week before admission, and five days before entrance he had a massive hematemesis. During the trip to the hospital he developed a left hemiplegia. Physical examination showed a left sided paralysis and a marked pallor, and there were rigidity and tenderness in the epigastrium. The hemoglobin was 75 grams. The patient became weaker

and died four days after admission. Autopsy revealed gastrojejunal ulcer with perforation into the left transverse mesocolon and localized abscess, recent and old encephalomalacia with hemorrhage, and terminal pneumonia.

**Comment.** We believe the reason for the recurrent ulcer in this patient is the same as that given for Case 50.

#### REPORT OF 121 ADDITIONAL GASTRIC RESECTIONS PERFORMED DURING 1944 AND 1945

During the past two years, 1944 and 1945, we have performed gastric resection in an additional 121 patients for peptic ulcer or its complications. Sufficient time has not elapsed for a detailed report to be of value, but a brief survey of these cases is of interest.

Forty-one, or 33.8 per cent, of these patients had had previous surgery for peptic ulcer. In 11 severe cases, or 21.5 per cent, the indication for resection was a severe complication of peptic ulcer or of previous inadequate surgical treatment. The indications for resection in these complicated cases were: recurrent ulcer with or without emergency resection for massive hemorrhage, seven; esophagogastric intussusception and perforation, one.

There were no operative deaths in the 121 patients, an immediate mortality of 0 per cent. We attribute the continued decrease in operative mortality to improvements in operative technique and careful attention to pre- and postoperative care. Two-thirds or more of the stomach was removed in a greater proportion of these patients than in the previous 100 patients.

We have been able to carry out follow-up examinations, including gastric analysis in 92 per cent of the patients. Although the follow-up interval has been short, varying from three to twenty-seven months, no recurrent ulcers have developed.

There were two gastroenterostomies performed for peptic ulcer during the period in which these 121 gastric resections were done.

#### CONCLUSIONS

1. Our postoperative mortality has been reduced from 25 per cent in the first fifty gastric resections to 5 per cent in the second series of 100 consecutive resections. It was further reduced to 1.6 per cent in 121 consecutive resections done in 1944 and 1945. Over the five-year period, 1941 to 1945 inclusive, the mortality was 15 per cent.

2. Radical resection of the stomach per se did not increase the mortality rate.

3. We have extended our indications for resections in peptic ulcer, as evidenced by the increasing number of resections performed.

4. The symptom of bleeding occurred in a greater per cent than we had anticipated.

5. Chronic invalidism induced by peptic ulcer is more common than we had realized.

6. In this study "irremoveable" duodenal ulcers were rare.

7. Our rate of recurrent ulcer has been reduced from 14.7 per cent in the first fifty gastric resections to 4.3 per cent in the ninety-two survivors of the 100

resections studied in detail. There are no known recurrent ulcers in the 119 survivors who were resected in 1944 and 1945. For the five years, 1941 to 1945 inclusive, the recurrent ulcer rate was 1.69 per cent.

8. Recurrent ulcer was more frequent after conservative than after radical resection.

9. A relative achlorhydria is necessary to prevent recurrent ulcer.

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## CONGENITAL HYPERTROPHIC PYLORIC STENOSIS

JOHN T. AKIN, JR., M.D., ATLANTA, GA., AND

GILBERT B. FORBES, M.D., ST. LOUIS, MO

*(From the Departments of Surgery and Pediatrics, Washington University School of Medicine, and the St. Louis Children's Hospital)*

**D**URING the past thirty years, certain principles have been evolved for the management of babies with congenital hypertrophic pyloric stenosis. As a result of their wide application, the mortality from this disease has fallen from the appalling figure of between 50 and 75 per cent to the point where one author<sup>1</sup> could state that he had operated on 134 consecutive patients without a fatality. While many clinicians are in general agreement as to the proper management of these cases, discussions of the relative merits of various treatment regimes continue to appear in the literature. Instances of mismanagement still occur with sufficient frequency to warrant continued emphasis on those practices which safeguard the welfare of these patients. Herein is presented a study of the 147 patients with congenital hypertrophic pyloric stenosis seen at the St. Louis Children's Hospital during the twelve-year period from 1933 through 1944. Earlier discussions from this clinic on the subject of pyloric stenosis are to be found in the papers of Hartmann,<sup>2,4</sup> McGhee,<sup>3</sup> and Clopton and Hartmann.<sup>5</sup>

In this series 81.7 per cent of the patients were males, 52.5 per cent of the male and 55.5 per cent of the female patients were first-born children. There were three instances in which two infants in the same family had pyloric stenosis. Of all the patients, 2.25 per cent were Negroes, whereas Negroes constituted 8 per cent of the total hospital population during the period of this study. The relative infrequency of the disease in the Negro can best be appreciated by the fact that during the eight years in which the Homer G. Phillips Hospital, a large Negro hospital in St. Louis, has been in existence, only one instance of congenital hypertrophic pyloric stenosis has been recorded at that institution.\*

The frequency of complicating congenital anomalies in our series was low. One patient had a double harelip and cleft palate, two had congenital heart disease, and one was a mongoloid imbecile. Significant congenital anomalies were not evident in the other 143 patients.

### DIAGNOSIS

Of the several important symptoms of pyloric stenosis, and the one which usually first attracts the physician's attention, vomiting is the most prominent. It begins with sufficient frequency in the first two weeks of life (Fig. 1), so that this disease should be included among those responsible for vomiting in

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\*Courtesy of Dr. Dorothy Jones, Chief Pediatrician at Homer G. Phillips Hospital.

the newly born.<sup>2</sup> Although the vomiting is often of a mild nature for the first few days, it rapidly becomes more severe and more frequent, and relatively soon assumes typical characteristics in most cases. The vomitus is strongly acid and does not contain bile. The vomiting is projectile, occurs frequently, and tends to persist despite therapeutic methods ordinarily effective in the control of vomiting due to gastroenterospasm and improper feeding.

Most of the other symptoms of pyloric stenosis are a direct result of vomiting and, therefore, occur with considerable regularity. The infant usually passes only one or two small stools per day; these are small in volume and suggest true constipation. He seems to be always hungry; he continually sucks his fists and takes feedings very eagerly. Despite a variety of formulas and feeding methods, he fails to gain weight properly and, if the stenosis is not relieved, will soon begin to lose weight at an alarming rate. As though puzzled by his inconsiderate stomach, the baby often develops a characteristic frown.

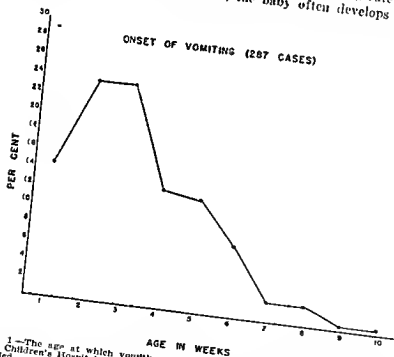


Fig 1—The age at which vomiting began in patients with pyloric stenosis seen at the St. Louis Children's Hospital from 1910 through 1914. The 110 patients reported by McGhee<sup>4</sup> are included.

As a consequence of vigorous peristaltic movements, the stomach wall becomes hypertrophied. Visible external evidence of this is seen in the waves of gastric peristalsis, which pass from left to right across the epigastrium. These become more prominent immediately after feeding and, with a proper tangential lighting effect, can be visualized in every case of pyloric stenosis. They can easily be distinguished from the waves of lower intestinal obstruction far, in the latter, waves are often visible in other parts of the abdomen.



and have no constant pattern of movements. Because of thinning of the abdominal wall, gastric peristaltic waves are seen in many malnourished babies, however, and, therefore, cannot be considered pathognomonic of pyloric stenosis.

The hypertrophied pylorus can commonly be felt as an almond shaped tumor just beneath the right lobe of the liver. A definite tumor could be palpated in 76 per cent of our patients. Several surgeons of wide experience have stated that under ideal conditions a tumor can be felt in every patient. Yet on more than one occasion in our series of cases, the hypertrophied pylorus was so situated, high under the liver edge, that it was impossible to feel it at time of operation through the abdominal incision. The presence of a tumor is pathognomonic of pyloric stenosis, but inability to feel it should not deter the physician from making the diagnosis and from instituting treatment.

Despite the regularity of vomiting in pyloric stenosis, *gastric retention* is a rather constant feature. This can be demonstrated by giving the baby a barium meal\* and observing its course under the fluoroscope. Observations should be made every fifteen minutes during the first hour and then at half-hour intervals until three hours have elapsed following the test meal. In normal infants a small amount of the fed barium will be seen to pass into the small bowel within fifteen minutes, and the stomach will usually completely empty itself within the three-hour period. In contrast to this, the stomach of a baby with pyloric stenosis will be seen to be considerably enlarged and to exhibit a *delayed emptying time*: barium will not leave the stomach until thirty or sixty minutes have elapsed, and at the end of three hours usually about one-half of the fed barium will still be seen in the stomach. Barium studies were done on 115 of our patients, including all those in whom a pyloric tumor was not felt. Only five patients failed to show a delayed emptying time of the stomach, and in one of these the emptying time was typically delayed when the procedure was repeated four days later. It should be remembered that a delayed emptying time will be seen occasionally in infants ill from other causes and that barium studies should be used only to confirm the diagnosis of pyloric stenosis.

The persistent vomiting produces other important effects. Since the stomach of the baby suffering from pyloric stenosis continues to secrete gastric juice of normal acidity, great quantities of hydrochloric acid are lost. This leads readily to deprecation of the blood chlorides which in turn results in a compensatory increase in bicarbonate content. The wastage of ingested food through vomiting also allows the body to become depleted of protein and of water. *Three important results occur: alkalosis, malnutrition, and dehydration.* The intensity of each of these phenomena varies directly with the length of time the disease has been allowed to progress.

Alkalosis manifests itself clinically in the form of *irregular shallow respirations* and frequent periods of *apnea*. *Tetany* may occur. Because of the fact that these patients are very young infants, tetany will usually be manifested, not by carpopedal spasm, but by generalized muscular rigidity and occasionally by a convulsion. The presence of alkalosis may be confirmed only by

\*One teaspoon of barium sulfate to one ounce of milk or formula.

making an analysis of the blood serum for its carbon dioxide content, which is largely a measure of bicarbonate. In metabolic alkalosis this will be elevated to a varying degree from the normal value (for small infants) of 50 to 60 volumes per cent. Analysis of the urine for its chloride content may be of help, for the chlorides (by the silver nitrate test) are usually absent from the urine of patients with pyloric stenosis. As Hartmann and Smyth<sup>7</sup> pointed out, the pH of the urine in this disease does not always reflect the bicarbonate content of the blood but depends rather upon the total osmolar concentration. If the sum of the bicarbonate and chloride contents of the blood serum exceeds that which obtains in the blood of a normal individual, sodium bicarbonate will be excreted in the urine, and the urine will then be alkaline. Due to the fact, however, that the vomitus of patients with pyloric stenosis contains an appreciable amount of sodium chloride in addition to hydrochloric acid, a considerable loss of base as well as chloride may occur, resulting in a reduction of the sum of the bicarbonate and chloride contents of the blood serum below the normal value. Under such circumstances the body tends to conserve base by excreting an acid urine. Obviously, then, the urinary pH is not an accurate indication of the presence or absence of alkalosis in patients with pyloric stenosis.

To illustrate the frequency and degree with which alkalosis occurred in this series, Table I, which correlates the blood chemical findings of our patients on admission to the hospital with the duration of vomiting, has been prepared.

TABLE I

	DURATION OF VOMITING IN DAYS				
	1 TO 7	8 TO 14	15 TO 21	22 TO 28	OVER 28
Serum CO <sub>2</sub> Content (Vol. %)					
Less than 50	0	0	3	2	1
50 to 70	12	12	4	1	0
70 to 90	3	14	12	2	6
90 to 110	0	4	3	1	11
Over 110	0	0	2	3	4
Serum Chloride as NaCl (Mg. %)					
550 to 650	2	10	6	2	5
450 to 550	6	19	8	1	5
350 to 450	1	4	4	5	10
250 to 350			2		2
Below 250				1	2

There is a rough correlation between the duration of vomiting and both the increase in bicarbonate and the reduction in chloride content of the blood serum. In prolonged cases however this relationship may no longer exist, for starvation and dehydration may become sufficiently marked, and anhydremia may sufficiently impair renal function, so that complicating factors enter the picture. For example a great extension of bicarbonate may be considerably checked through the accumulation of organic acids, the retention of sulfate and phosphate, and an increase in protein. Likewise, a low chloride value may be elevated by reduction in the water content of the blood serum through dehydration. This phenomenon is illustrated in the fifth column

of Table 1, in which it can be seen that a number of the values for bicarbonate fall in the normal or slightly elevated groups and that a considerable number of the chloride values are in the normal or moderately depressed groups.

Some indication of the degree of dehydration in these patients and the amount of attendant renal insufficiency is given by the values for serum non-protein nitrogen obtained on admission to the hospital. Of the thirty-six patients for whom such values were recorded (which includes most of the severe cases) twenty had elevated nonprotein nitrogen values; ten of these were in the range between 35 and 50 mg. per cent; nine were between 50 and 100 mg. per cent, and one was 112 mg. per cent. The azotemia promptly disappeared upon relief of dehydration and resumption of adequate urinary flow.

The continued occurrence of vomiting, especially if it is projectile in nature, is frequently a factor in the production of otitis media in young infants. In this series, 13 per cent of the patients had otitis media on admission to the hospital, and 10 per cent subsequently developed it during their post-operative convalescence.

Other complicating infections present in our patients on admission were one instance of pyelitis, three of acute pharyngitis, four of generalized upper respiratory infection, and one of suppurative cervical adenitis. Complications met with during the postoperative period were one instance of pyelitis and colon bacillus sepsis, three of bronchopneumonia, one of bronchitis, two of pertussis, and one of exanthema subitum.

#### TREATMENT

The analysis by McGee of those cases of pyloric stenosis seen at this clinic from 1916 through 1932 established the superiority of the surgical over the medical treatment of this disease. All of the patients in this present series were subjected to operation, with the exception of four patients who died before they could be made ready. The only occasion in which a medical regime of therapy seems at all feasible is in those patients who are first seen at the age of 3 months or more and whose nutritional status is sufficiently good to presuppose a relatively mild degree of stenosis of the pylorus.

*Preoperative Care*—Preoperative therapy has the following aims: (1) the restoration of normal electrolyte and fluid balance, (2) the amelioration of malnutrition, and (3) the control of complicating infections. We should like to emphasize that these considerations are of the utmost importance and that they should be satisfied, in so far as is possible, before any surgical procedure is undertaken. Congenital hypertrophic pyloric stenosis is not a surgical emergency, and far more harm may come from operating hurriedly upon an ill-prepared patient than by waiting two or three days until conditions are optimal. In instances where the diagnosis is made early in life, the baby's condition may be such that almost no preoperative therapy is required or at the most one or two subcutaneous infusions of Ringer's or saline solution. However, in a large majority of our patients this was not the case. Less than one half of our patients were admitted to the hospital within two weeks of the

onset of symptoms, and fully one-fifth of them were not brought to us until from one to two months had elapsed. In some of the more severe cases the patients required from four to six days of preparation before they were considered fit for operation.

The first two aims of preoperative therapy—the restoration of normal electrolyte and fluid balance and the amelioration of malnutrition—involve the following considerations: (1) the correction of alkalosis, (2) the correction of hypochloridemia, (3) the abolition of dehydration, (4) the relief of hypoproteinemia and anemia, (5) the augmentation of liver glycogen reserves, and (6) the minimization of starvation during the preoperative period. Although small oral feedings, offered at frequent intervals, are given during the preoperative period, it is obvious that all of these aims must be met via the parenteral route. They can be accomplished most easily and simply in the following ways.

(1) The repeated intravenous administration of 10 per cent dextrose in saline or Ringer's solution in amounts of 20 cc per kilogram of body weight. If this procedure must be repeated frequently, 10 per cent dextrose in water should occasionally be substituted in order to minimize the occurrence of edema.

(2) The repeated subcutaneous or intraperitoneal infusion of Ringer's solution in amounts averaging 100 cc per kilogram of body weight per day.

These procedures will relieve dehydration, restore glycogen reserves in the liver, reduce hypochloridemia, and establish diuresis so that the kidney through its wonderful capacity of selective reabsorption can excrete sufficient sodium bicarbonate to attenuate the alkalosis. Once the patient has been well hydrated, the following steps should be taken.

(3) The transfusion of whole citrated blood or of plasma, according to the blood hemoglobin value, in amounts of 20 cc per kilogram of body weight. Equivalent amounts of concentrated serum albumin may be substituted for blood plasma.

(4) The subcutaneous administration of a solution composed of 3.3 per cent dextrose and 3.3 per cent Amigen in one-third Ringer's solution\* in amounts approximating 100 cc per kilogram of body weight per day.

Thus hypoproteinemia is corrected, calories provided, blood volume restored to normal, and kidney function stimulated to reduce further the alkalosis. This regime is continued until the blood serum carbon dioxide content, chloride, and protein values are approximately within normal limits and will suffice to prepare adequately for operation the great majority of these patients. However, in those patients in whom fluid and electrolyte changes are severe and starvation marked, several other measures may be necessary. The correction of a severe alkalosis, which may result in tetany, convulsions, and such reduction in respiratory excursions that death is imminent, often will require the following additional measures.

(5) The inhalation of 30 per cent carbon dioxide in oxygen. By increasing the carbon dioxide tension of the blood, the blood pH will be lowered

\*"D-A-R" solution: this can be made up easily by mixing equal parts of 10 per cent dextrose, 10 per cent Amigen, and ordinary Ringer's solutions.

temporarily and breathing stimulated. Continuous oxygen therapy is often of great help.

(6) The intravenous injection of 5 per cent calcium chloride in amounts of 0.5 c.c. per kilogram of body weight. An excess of calcium is thus made available to augment that portion of the blood calcium rendered non-ionizable because of the alkalosis, and an acidifying action is produced by virtue of the fact that the calcium is excreted to a large extent through the bowel, thus leaving the chloride ion available for combination with base from bicarbonate in the blood.

(7) The intravenous injection of hydrochloric acid, as reported by Hartmann.<sup>3,4</sup> The response to hydrochloric acid is prompt, but it has the disadvantage of being extremely irritating to the blood vessel walls and must be given with the greatest of care. Because of its powerful acidifying action, it will quickly lower the blood pH, but this same attribute makes it difficult to inject sufficient quantities to elevate adequately the serum chloride. Hydrochloric acid has been given intravenously to four patients in this series. In two of them, respiratory failure occurred during the immediate postoperative period, the response to hydrochloric acid was dramatic and was definitely a lifesaving measure. In another it successfully relieved generalized convulsions and spasticity which had not been influenced by carbon dioxide inhalations or the intravenous administration of calcium chloride. The fourth patient had only slight improvement in symptoms from the use of hydrochloric acid because of the presence of a concomitant severe hypoglycemia. Following the intravenous administration of glucose, his respirations rapidly improved.

The solution of hydrochloric acid, as we have employed it, has been made up in various ways. In one patient, 1 c.c. of concentrated hydrochloric acid was diluted to 100 c.c. with Ringer's solution, and 20 c.c. of this mixture were given. In another, 3 c.c. of concentrated acid were mixed with 60 c.c. of Ringer's solution and 20 c.c. of the resultant mixture used. The third patient was given 170 c.c. of one-sixth molar hydrochloric acid in normal saline solution in three divided doses. In the fourth patient 40 c.c. of one-tenth normal hydrochloric acid were mixed with 70 c.c. of normal saline and the entire solution given. When these amounts are calculated on the basis of the strength of the solution used per kilogram of body weight for these respective patients, they are 10 c.c. per kilogram of one-tenth normal acid, 6 c.c. per kilogram of one-half normal acid, 60 c.c. per kilogram of one-sixth normal acid, and 37 c.c. per kilogram of one-seventeenth normal acid. Because of the obvious dangers of administering hydrochloric acid intravenously, it should be used only as an emergency measure in instances of severe alkalosis.

The third preoperative objective, that of control of complicating infections, must be achieved, for otherwise nutrition during both the pre- and postoperative periods may be greatly hampered. Further, since postoperative vomiting or diarrhea is occasionally a problem, anything which might possibly contribute to their occurrence should be corrected. The judicious use of the sulfonamide drugs and of penicillin should suffice to control most such infections.

*Anesthesia and Operative Procedure.*—A Fredet-Rammstedt pyloroplasty was performed on 143 patients in this series. Since twenty-four different surgeons, including both visiting staff and house officers, participated in the series, there has been some variance in preoperative medication, anesthesia, and finer points of operative technique. Since the technical details of this operation are now well known, we propose to discuss only those general features of special importance.

We believe that preoperative medication is not necessary, and our experience indicates that premedication with morphine may actually be dangerous. In eight of the eighty-three patients who received  $\frac{1}{60}$  to  $\frac{1}{120}$  gr. of morphine and were operated upon under local anesthesia, the immediate post-operative course was complicated by marked respiratory depression and generalized cyanosis. This complication has not been encountered in a single one of the sixty patients operated upon without premedication, and accordingly, we feel justified in concluding that the morphine was a major factor in the cause of the respiratory depression. Further, we prefer not to use atropine, which often causes an annoying flush and elevation in temperature.

We are in full agreement with Ladd and Gross\* that drop ether is the anesthetic of choice, and we have experienced no complications attributable to ether anesthesia in this series. So little ether is required for the satisfactory quieting of these infants that in every instance they have awakened before leaving the operating room. There seems to be little advantage in employing a local anesthetic since in an appreciable percentage of cases it is necessary to use supplementary ether anesthesia when the peritoneum is opened or during closure of the wound because of annoying and dangerous movements of the patient. Moreover, the only two instances of delayed wound healing in our 143 patients operated upon occurred in those in whom a local anesthetic (novocain) was used.

Before the abdominal wound is closed, the operator should assure himself that the mucosa of the duodenum is intact. In our series the duodenum was inadvertently opened in twelve patients. In eleven of these the perforation was recognized at operation and closed with interrupted fine silk or catgut sutures; as a consequence, their postoperative courses were uneventful. In the other case the opening was not discovered, and the patient succumbed to a generalized peritonitis.

*Postoperative Care.*—The infant should be offered food within a few hours after the effects of the anesthetic have worn off, so that the earliest possible start is made toward regaining a normal nutritional status. The food should provide sufficient calories yet require a minimal amount of digestive activity and be absorbed easily through the intestinal wall. Because the stomach is actually hypertrophied as well as dilated, gastric motility may still be impaired despite the presence of an adequate pyloric lumen. Consequently, the food should be of the type which passes readily from the stomach into the small intestine. One of the most serious complications during the postoperative period is that of diarrhea, the occurrence of which can be minimized by the use of an acid feeding.<sup>2</sup>

The following feeding schedule meets these requirements nicely. About two hours postoperatively the infant is offered 15 c.c. of a mixture composed of equal parts of 10 per cent dextrose, 10 per cent amigen, and buffer water\* (D-A-B). Two hours later he is offered alternate feedings at two-hour intervals of 15 c.c. of D-A-B and 15 c.c. of a formula composed of one part evaporated milk, one part water, and one part of a 1 per cent lactic acid-15 per cent Karo mixture. The next day the amounts are increased to 30 c.c. and the next to 60 c.c. per feeding. On the fourth postoperative day, D-A-B is omitted, and the milk formula is offered every three hours in 90 c.c. amounts. Further feedings are adjusted individually to the patient, but by the tenth postoperative day the infant is usually taking 120 c.c. of a fairly concentrated acidified evaporated milk formula every four hours. If breast milk is available, it may be substituted for the evaporated milk formula in this feeding schedule and the baby put to breast on the second or third postoperative day.

If we take as an example a 7-week-old infant, whose ideal weight would be 4,500 grams, the amounts of calories, protein, carbohydrate, and fluid as shown in Table II would be supplied by this feeding regime.

TABLE II

POSTOPERATIVE DAY	CALORIES PER KG.	PROTEIN (GM. PER KG.)	CARBOHYDRATE (GM. PER KG.)	TOTAL FLUID (C.C. PER KG.)
1	145	1.1	23	40
2	370	2.2	46	80
3	740	4.4	92	160
4	1060	3.7	133	160

It is obvious that it is only the first two postoperative days in which supplementary parenteral feeding and fluid in the form of Ringer's or dextrose-amigen-Ringer's solutions will be needed.

## DISCUSSION

Eight of the 147 patients in this series died, which is a mortality rate of 5.4 per cent for the twelve-year period covered by this study. Four patients died prior to operation, so that the mortality for the group of patients operated upon is 2.8 per cent.

Three patients died from the effects of severe alkalosis and malnutrition. At the time they were admitted to the hospital they presented the picture of marked malnutrition and dehydration with subnormal temperature, cyanotic color, and irregular breathing. They weighed from 800 to 1,500 grams less than their respective birth weights. The serum carbon dioxide contents were above 100 volumes per cent and the serum chlorides below 325 mg. per cent in each. Despite vigorous attempts to correct these conditions, they all succumbed within three days. Surgical exploration in these cases would have been most foolhardy, for any operative procedure would certainly have hastened the deaths. An autopsy was done on two of the patients and, except for the typical hypertrophied pyloric muscle, revealed only mild terminal bronchopneumonia.

\*Buffer water: a mixture of 1 per cent lactic acid and 0.5 per cent sodium-r-lactate

The importance of proper control of the biochemical factors in this disease is further amplified by our experiences with two patients in whom alkalosis and hypochloridemia had not been properly corrected prior to operation. Local anesthesia and morphine premedication were employed in each, and both of them suffered such marked respiratory depression postoperatively that without the prompt intravenous administration of hydrochloric acid, death would have occurred. The extent of the biochemical change in patients with pyloric stenosis is also of some prognostic significance, for of the five patients in this series whose serum chlorides were below 300 mg. per cent on admission to the hospital, three died before they could be prepared for operation.

The dangerous potentialities of atropine are evident from a study of the fourth fatal case. This baby was in excellent general condition at the time of admission to the hospital, and because the symptoms had been mild, it was decided to employ a regime of medical therapy. After three days of therapy with atropine and thickened feedings, he developed massive gastric dilatation which, though relieved by gastric lavage, recurred the following day and was followed by gastric perforation, peritonitis, and death. Such an experience serves to emphasize a cardinal rule in the therapy of pyloric stenosis: never postpone surgical treatment beyond the period needed to prepare the patient for operation once the diagnosis has been definitely established. Despite our firm conviction that pyloroplasty is the treatment of choice, we have on several occasions employed one of the various schemes of medical therapy which are advocated from time to time. The result has always been the same: operation was eventually required, and frequently the postoperative convalescence has been longer than usual because of the occurrence of some intercurrent infection or diarrhea.

Two patients died of complicating infections during the postoperative convalescence. One, seen in the period before the sulfonamide drugs were available, had an otitis media on admission to the hospital and subsequently developed a bronchopneumonia and expired on the ninth postoperative day. The other developed a colon bacillus pyelitis and sepsis and, despite the use of sulfanilamide, expired on the twentieth postoperative day. Now that more powerful sulfonamide drugs and penicillin are available the number of fatalities from concurrent infections should be considerably reduced. Such therapy should be employed promptly in all instances of concurrent infections in these patients, however trivial such infections may appear at the onset.

The seventh fatality represents the only instance in this series in which a duodenal perforation was overlooked at the time of operation, and death came as a result of generalized peritonitis. In the eighth fatal case, two Fredet-Rammstedt pyloroplasties done three weeks apart failed to relieve the patient's symptoms, nor did a posterior gastrojejunostomy done three days later do so. Despite these procedures and vigorous supportive therapy, the baby became progressively worse, blood appeared in the vomitns, convulsions and cyanosis developed, and death occurred four days after the last operation. An autopsy revealed that both the pyloric and gastroenterostomy lumina were



patent and that there was some bronchopneumonia in all lobes of the lungs. Examination of the spinal fluid during life was normal, but unfortunately permission was not granted to study the brain at autopsy.

#### SUMMARY

One hundred forty-seven consecutive cases of congenital hypertrophic pyloric stenosis seen at the St. Louis Children's Hospital during the past twelve years are reviewed.

The important diagnostic features of the condition are discussed and the value of proper preoperative therapy emphasized, particularly the correction of disturbances in acid-base and fluid balance, the amelioration of malnutrition, and the control of complicating infections. The use of amigen in the therapeutic scheme is outlined.

Early surgical treatment using drop ether anesthesia is advised. Morphine as a premedication is contraindicated.

The cause of death in the four preoperative and four postoperative cases is discussed briefly.

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## LESSONS OF THE AMPULLA OF VATER

HUBERT L. BAKER, M.D., AND DORIS W. CALDWELL, M.D., CHICAGO, ILL.

(From the Presbyterian Hospital of Chicago)

THIS report will concern itself with four different lesions of the ampulla of Vater which have been observed in the past three years. The conditions are (1) cystic dilatation of the common bile duct, (2) benign papilloma of the ampulla, (3) adenocarcinoma of the ampulla and (4) ulcer of the duodenum affecting the ampulla. A description of each of the conditions listed here will be made in the order stated. Following a short historical résumé of the conditions in question, a specific case representing each of the lesions named will be discussed.

### CYSTIC DILATATION OF THE COMMON BILE DUCT

Cystic dilatation of the common bile duct is of such rarity as to make it advisable to report all such cases. It is well to recognize that only at operation can such conditions be regularly differentiated from the more frequent, less hopeful malignant neoplasms.

From the present number of approximately 250 such cases, the following brief facts are known. The condition appears almost entirely in childhood or young adulthood, and is most frequent in females below the age of 25 years. Rolleston<sup>10</sup> suggested the causes of cystic dilatation were (a) idiopathic—that is, no obvious obstructions, and considered due to a primary inherited weakness of the wall of the duct, (b) obstruction at the distal end of the common duct as by congenital stricture, trauma, stones or surgery, infections such as syphilis, typhoid, and a more heterogeneous group of bacteria from the intestine. The condition is accompanied by symptoms<sup>11, 12</sup> and findings, as recurrent jaundice and occasionally paroxysmal pain. Rolleston<sup>10</sup> and Jelks<sup>11</sup> described two cases of great dilatation of the common duct producing gigantic thin-walled cysts. These were considered idiopathic in nature. In 1943, Brooks and Weinstein<sup>13</sup> described a large, multilocular cyst in a duodenal diverticulum producing symptoms of acute cholecystitis. The cyst was found on section to be lined with duodenal rather than cholelochoous mucosa.

CASE 1 (Hosp. No. 412248):—A 68 year old Scottish woman had been in the Presbyterian Hospital twelve years previously for arthritis, migraine, and intercostal neuralgia. On this first admission, she had given a history of occasional mild right upper quadrant distress. The history of her presenting complaints were: Since August, 1943, she noted a continuous darkening of the urine without blood, and the stools were of clay color. She lost her appetite and began to lose weight. In September, 1943, she began to have right upper quadrant pain, radiating to the right sub-epicardial region and across anteriorly to the left upper quadrant. The pain was intensified by fats and lasted minutes to hours. Nausea was present in the absence of pain. There was no emesis. At no time had there been fever or chills. Other than these, the systematic inventory was relatively negative. Physical examination revealed the following pertinent facts. The patient was extremely jaundiced, dehydrated,

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and weighed 150 pounds. Blood pressure was slightly elevated. Respirations and pulse were normal. Temperature was 98.5° F. The heart findings were consistent with the elevated pressure. The liver was palpable 8 cm. below the right costal margin with the question of a small, irregular, hard mass on its tender, free border. The kidneys and spleen were not palpable. There was no rigidity or scars.

The differential diagnosis at this time was regurgitation, jaundice of an obstructive type due to malignant neoplasm of the common duct or of the pancreatic head, metastatic carcinoma of the liver, and arteriosclerotic, with hypertensive cardiovascular disease.

Treatment instituted was analgesics, vitamins K and C parenterally, high multivitamin, high carbohydrate, low fat, low protein diet, and proposed surgical exploration.

Preoperatively, the positive laboratory findings were soft, formed clay-colored stools and urine 2 plus albumin in which bile was present. The serology was negative. There was slight anemia. Icteric index was 102. Van den Bergh test was direct, immediate, and positive. Prothrombin level was 100 per cent. Roentgenography demonstrated a nonfilling gall bladder, without stones (Fig. 1).

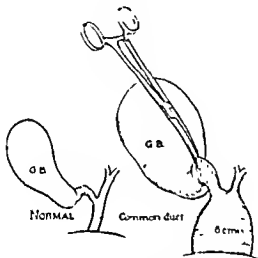


Fig. 1—Left normal, right enormously enlarged gall bladder, equal not common ducts.

At operation the liver was greatly enlarged, bronze copper in color. The gall bladder was markedly distended, without stones. The common duct (see Fig. 1) was very large, 4 to 6 cm. in diameter. The walls of the duct were only moderately thickened. The gall bladder was explored and aspirated a very thick, viscid, black bile. The common duct was opened and thoroughly explored without evidence of obstruction. There was a firm nodule felt at the head of the pancreas about 0.5 to 1.0 cm. in diameter which did not seem to encroach on the common duct. The duodenum was opened, the ampulla of Vater, identified, and a catheter was inserted into the common duct. No obstruction was found. The gall bladder was anastomosed to the pyloric end of the stomach. The common duct and duodenum were closed. A drain was placed in the right kidney fossa. The peritoneum and abdominal wall were closed in the usual manner.

Without biopsy, a tentative diagnosis was made of malignancy of the head of the pancreas and congenital enlargement of the common duct.

Fourteen days after operation, the stools and urine were normal. Icteric index was 21. The patient left the hospital ambulatory on the forty first postoperative day.

The patient was observed ambulatory from April 12, 1944, to Dec. 21, 1945. During this period of observation, there was a gradual increase of jaundice, constipation, and upper

abdominal pain radiating to the left shoulder. Hemoglobin was stabilized at 65 per cent. In December, 1945, she was readmitted to the hospital with a marked accentuation of transepigastric pain, formed light yellow to clay colored stools, an inability to eat fatty foods, a generalized pruritis, and bile stained urine. A nodular liver with a tender caudate lobe was palpable below the right costal margin. Hemoglobin was 62 per cent; red blood cells, 3.52; icteric index, 76; prothrombin, 75 per cent, Van den Bergh immediate, direct, positive. Two weeks later the icteric index was 100 and the Hangar test negative at the end of forty-eight hours. Two weeks after this icteric index was 137, at which time the patient was discharged from the hospital with poor prognosis. The diagnosis at this time was neoplasm at the head of the pancreas with metastasis to the liver and obstruction of the bile ducts.

**Summary.**—The case presented here has certain interesting relationships with and contradictions to the facts mentioned in the historical résumé, such as the advanced age of the patient and the apparent idiopathic nature of the dilatation in the absence of a demonstrable obstruction unless one considers that the tumor nodule at the head of the pancreas produced the obstruction.

In addition, this patient had symptoms which should be differentiated from stones in the duct and carcinomas and papillomas of the ampulla, therefore, an exploration of the ampulla is indicated in any case of bile duct obstruction.

#### BENIGN PAPILLOMAS OF THE AMPULLA OF VATER

Because the greater number of the reports on tumors of the ampulla of Vater has been concerned with malignancies primarily in this region,<sup>3, 7, 9, 13, 15, 16, 20, 22</sup> one comes to the conclusion that the majority of tumors of the ampulla are malignant, however, a few cases of benign ampullary tumors have been observed.<sup>6</sup> The importance of these benign lesions is obvious inasmuch as their differentiation from early malignant growths is not possible except at the time of surgical exploration. The further importance of such tumors is to be emphasized when one realizes that 70 per cent<sup>13</sup> of the also rare<sup>16</sup> carcinomas of the duodenum are at the ampulla.

The first known recorder of these benign tumors was Bouisson,<sup>6</sup> who in 1843 described what was apparently a lipoma of the ampulla in a cadaver. Since this time, there have been reported approximately seventy clinical cases.

In 1939 Christopher<sup>6</sup> listed forty-one cases. In order of frequency, there were papillomas, adenomas, lipomas, fibromas, neuromas, granulomas, melanoma, and carcinoid. Only six of these cases were known definitely to involve the ampulla.

Up to October, 1936, there had been only twenty-five cases of benign tumors of the bile ducts found by the Mayo Clinic during 34,000 operations on the biliary passages.

In 1937 Brunschwig<sup>6</sup> successfully operated on a carcinoid of the ampullary region.

**Papilloma as the Precursor to Carcinoma of the Ampulla of Vater.**—Accepted by some is the belief of Rolleston<sup>20</sup> that primary carcinomas of the region of the Ampulla of Vater start as benign papillomas. This is because of the similarity<sup>6</sup> of the gross and microscopic appearance of benign tumors to the low-grade papillary carcinomas. MacCarty<sup>12</sup> raised the question as to the possi-

bility of ulceration of the periampullar duodenum being the precursor of such malignancies. He reported three such ulcerocarcinomatous cases in 1910. The statement by Mayo Robson<sup>17</sup> that calculi in the common duct are causes of papilloma or carcinoma is a debatable one.

*The Nature of the Papilloma About the Ampulla of Vater.*—Most of the papillomas are of a columnar epithelial type and not of glandular formation. This is in contradistinction to the adeno type of formation of the carcinomas. The tumors are usually very small. They may be cystic or solid<sup>18</sup> and consist usually of small hard white masses, often readily mistaken for an impacted calculus or a carcinoma.

*Common Symptoms and Findings of Tumors of the Ampulla of Vater.*—The most common symptoms and findings are those of painless jaundice, generalized pruritis, weight loss (due, according to Hunt,<sup>19</sup> to retention of bile and loss of external pancreatic secretion), hepatomegaly, fever, and diarrhea.

CASE 2 (Hop No 410117).—A 49 year old Italian man, up to five months previous to admission, had been in perfectly good health. He then noted a yellowness of the sclera, consulted a doctor, and, although gall bladder studies showed absence of stones, but no visualization surgical treatment was not advised. The scleral jaundice persisted one month, then disappeared, but recurred one month before admission, persisting until after operation. During the last icteric period, a generalized itching, becoming progressively worse, occurred. In the four months previous to admission, he experienced anorexia and a twenty five pound weight loss. Stools had been at times acholic, at other times normal in color, but pasty in consistency. He had not noted the urine color. At no time had there been any pain, fever, or chills.

Past history and systemic inventory were negative other than for the facts given.

Physical examination revealed an Italian man, deeply jaundiced. Temperature was 99.8° F., respirations, pulse, and blood pressure were normal, the abdomen was slightly rigid and distended, a firm, movable mass was palpable 6 cm below the right costal border. It was smooth and not tender, with a sharp margin. The spleen and kidneys were not palpable. There was no rectal abnormality.

A tentative differential diagnosis was (a) carcinoma of the head of the pancreas, involving the ampulla of Vater, (b) toxic hepatitis, (c) biliary cirrhosis, (d) primary hepatic malignancy, or (e) metastatic hepatic malignancy.

Treatment advised was high vitamin, high carbohydrate, low fat, low protein diet; vitamins C and K parenterally, surgical exploration.

Before operation the pertinent laboratory findings were formed clay colored stools, positive for chemical blood. Gross fat, bile, meat fibers, and parasites were absent. Urine was dark but otherwise normal. Serology was negative. There was slight hyperchromic anemia. Leucocyte count was normal. Icteric index was 67; van den Bergh was direct, immedial, positive. Prothrombin was 100 per cent. Hanger's test was negative at twenty-four hours, 4 plus at forty-eight hours. Roentgenography showed a nonfilling gall bladder without stones.

At operation the gall bladder was greatly distended to ten times its normal size. There were glands along the gastrohepatic omentum. Aspiration produced no stones from the gall bladder, which was explored. The head of the pancreas was only slightly thickened. When the duodenum was opened, a papillomatous mass protruded through the ampulla. Immediate frozen microscopic section of the curetted tumor was reported as benign as was an adjacent gland in the hepatic omentum. The gall bladder was anastomosed to the opening of the duodenum. Due to the patient's severe jaundice, resection of the ampulla at this time was deemed unwise. The incision was closed in layers after placing a drain in the right kidney fossa. The patient was returned to his room in good condition. The stools and urine



Fig 2—An overgrowth of glandular epithelium with slightly increased staining power. This is a portion of a papillary piece of tissue removed from the lining of the duodenum.

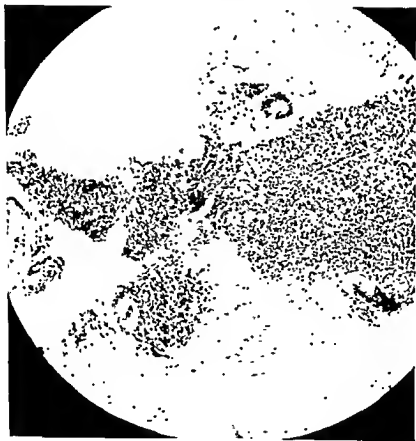


Fig 3—This specimen showing a benign overgrowth of glandular epithelium over a fibrous core.

became normal in a few days. The patient left the hospital ambulatory on the twenty third postoperative day (Figs. 2 and 3).

The patient was seen seven months after the operation. He felt fine and had gained twenty two pounds with no recurrence of jaundice or itching. The stools and urine remained normal. Sclerotic index was 12 and other blood chemistry tests were within normal limits. Gall bladder roentgenography at this time demonstrated a deformed duodenal cap and some irregularity of the second portion of the duodenum. There was no evidence of regurgitation of barium from the duodenum into the gall bladder.

The patient was seen two years later in excellent health, with satisfactory weight gain. X ray examination at this time showed no retrograde filling of the bile tracts. The conclusion was that the lesion was benign.

**Summary** - In view of the previous discussion as to the possibility of benign lesions being the precursor of malignancies of this region, the question might be raised as to whether or not it might have been advisable to remove the ampulla and reimplant the common duct and duct of Wirsung into the lower duodenum.

#### CARCINOMA OF THE AMPULLA OF VATER

Brunschwig<sup>1</sup> stated that Avezon<sup>2</sup> offered one of the earliest descriptions of carcinoma of the ampulla of Vater in 1875. He also referred to a report of such growths previously made by Perrot and Lutton in 1859. As previously mentioned, adenocarcinomas of the region of the ampulla of Vater are the most common of this area. However, Brunschwig<sup>2</sup> stated that ampullar carcinoma is relatively uncommon. According to Lieber, Stewart, and Lund,<sup>3</sup> there were 14 cases among 22,152 necropsies at the Philadelphia General Hospital between 1920 and 1936, and 4 cases at the Jefferson Hospital, Philadelphia, among 4,154 necropsies. This presents an incidence of 1.13 per cent of all carcinomas and 0.09 per cent of all autopsies. Roscher<sup>4</sup> noted 5 cases of ampullar carcinoma among 8,724 autopsies performed in this between 1900 and 1936. On gross examination in situ, these may readily be mistaken for small calculi or benign neoplasms. Therefore, as stated before, these must be most closely scrutinized and biopsy made if at all possible. Radical resection for this type of tumor was first performed in 1899 by Halsted.<sup>5</sup> Since this time many variations in the technique have been developed. For a review of such techniques one may refer to Brunschwig.<sup>6</sup>

**CASE 3 (Hosp. No. 416331).**—A 65 year old Polish man, a laborer, entered the hospital Feb. 9, 1944, complaining of one year's duration of chronic cough, for which no cause could be found. For seven months he had had an increasing generalized painless jaundice and a loss of ten pounds in weight. For two weeks stools had been loose and gray. At no time had there been anorexia, fever, chills, or itching.

The pertinent findings were generalized jaundiced skin and a slightly irregular, firm, movable mass extending 7 cm. below the right costal margin and 10 cm. below the middle third of the left costal border. There were small external hemorrhoids. The stool was acholic and pasty, with 5 plus occult blood. The urine contained urobilin. There was a mild secondary anemia. Roentgenography demonstrated a nonfilling gall bladder without stones.

After the usual preoperative preparations, the abdomen was opened. The liver was cirrhotic, atrophic, and about one half its normal size. A nodule which felt like a soft stone, but proved to be a neoplasm, was palpated 3 cm. above the ampulla in the duodenal lumen. The common duct was explored. There was some gravel but no stones. A catheter would not pass into the duodenum through the common duct. The duodenum was opened. The

ampulla was involved in a carcinomatous growth which was resected. Because of the absence of any bile, due to obstruction, the gall bladder was anastomosed to the stomach. The openings in the common duct and duodenum were closed. The patient survived seventy-two hours after the operation, death being due to a generalized peritonitis and hypostatic pneumonia (Fig. 4).

*Summary.*—In this case certain interesting observations are of note, namely, (a) the similarity of symptoms and findings with those of the two preceding cases, (b) the presence of the colorless fluid in the gall bladder, and (c) the cirrhotic nature of the liver.

The prognosis for recovery was, of course, poor due to the extensive liver damage as a result of the marked biliary obstruction. It would probably have



FIG. 4.—A typical overgrowth of glandular epithelium arising in the lining of the duodenum. On the right is the lining minus the desquamated covering of the epithelium, but the papillary stroma remains. The remainder of the specimen is loose fibrous tissue which is partially granulation tissue within which are glands of different sizes and shapes lined with epithelium increased in staining quality but still arranged fairly regularly and retaining its basal polarity. It was demonstrated in other parts of the surgical specimen that similar atypical glands were invading the submucosa and muscularis. This represents a low-grade (grade 1) adenocarcinoma. No pancreas is present in the specimen.



been better to have drained only the gall bladder at the first operation and then performed a more extensive operation at some future time with the patient perhaps in better condition

#### ULCER OF THE DUODENUM AFFECTING THE AMPULLA OF VATER

Ulcer of the duodenum affecting the ampulla of vater is a rather rare condition which may come about as a result of a primary ulcer in this region or as a result of marginal ulcers following various gastroedemic anastomoses for intractable ulcers of the stomach or first portion of the duodenum

CASE 4 (Hosp No 442892) — A 46 year old man entered the hospital in August, 1944, with a history of two years of intermittent epigastric pain but no jaundice. Roentgenography showed a nonfilling gall bladder without stones. The laboratory findings were not significant. At surgery a contracted gall bladder was found. There was no duct obstruction or dilatation of the ducts. Because of the small gall bladder it was drained. In December, 1944, due to a persistent draining biliary sinus tract and jaundice, exploration was again attempted. No stones were found in the ducts or ampulla. A T tube was placed in the common duct. Repeated diodrast studies failed to show any duct obstruction. The tube was removed after some months, and for a period of time there were occasional transitory pain, jaundice, and clay colored stools which persisted until November, 1945, when there was a severe intestinal hemorrhage with the finding after transfusion and vitamin K treatment of a duodenal ulcer which was treated medically until Jan 1, 1946. At this time laboratory findings of importance were icteric index of 50 and 4 plus occult blood in the stool. On Jan. 2, 1946, operation was again instituted at which time the common duct was opened and yielded green viscid bile. The duodenum was opened, and an ulcer  $\frac{1}{2}$  to 1 cm in diameter was found 3 cm above the ampullary ostium on the ventral side in the duodenal mucosa. The ulcer was incised and the edges were approximated. A choledochojunostomy was performed and a drain placed in the right renal fossa. The incision was repaired in the usual manner. The diagnosis at this time was (a) duodenal ulcer involving and obstructing the ampulla and (b) some anomalous condition of the biliary tracts not discernible at operation.

The patient made an uneventful recovery with an icteric index of 2, normal stools, a disappearing jaundice, and a weight gain of thirteen pounds three months later.

#### FINAL SUMMARY

Four cases have been presented, each of a different pathologic nature, but with marked similarity of symptoms and findings, such as persistent jaundice, pruritis, anorexia, weight loss, and stool color changes. Because of such similarities and the great difference in prognosis, the following conclusion is expounded: In those patients with biliary tract obstruction producing symptoms and physical findings which cannot be readily explained by the simpler, less hazardous means, the surgeon is thoroughly justified in exploring the ampulla of Vater transduodenally, and in agreement with Brunshwig's transduodenal resection with reimplantation of the ducts with, or in the absence of, internal biliary drainage should be the choice for ampullar carcinomas of 1 cm or less in diameter that appear quite circumscribed or show little gross evidence of infiltration and which do not extend into the pancreatic tissue.

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# ENTEROGENOUS CYSTS OF THE DUODENUM

## CASE REPORT AND REVIEW OF LITERATURE

THOMAS A. SHALLOW, M.D., FREDERICK B. WAGNER, JR., M.D., AND  
W. BOSLEY MANGES, M.D., PHILADELPHIA, PA.

*(From the Samuel R. Gross Surgical Division of the Jefferson Medical College Hospital)*

**D**ESPITE the rarity of enterogenous cysts of the duodenum, the surgeon should be capable of recognizing them and should be acquainted with the proper methods of treatment. Generally encountered unexpectedly at laparotomy these cysts may be confused with other lesions and their true identity may escape both surgeon and pathologist. The limited data available for discussion of this topic necessitate a complete review of the literature. We are also reporting a recently encountered case of our own, interesting because of successful treatment by a method usually not applicable.

The outstanding features of the case herewith cited are as follows: A 12-year old boy suffered recurring attacks of partial high intestinal obstruction since the age of 1 year and passed tarry stools just prior to admission. Abdominal examination was negative. Roentgen-ray study revealed an obstructive lesion in the duodenum. An enterogenous cyst of the duodenum was successfully treated by excision from within the lumen.

### CASE REPORT

**I.** A white male, age 12, was admitted to the medical ward of the Jefferson Medical College Hospital on Feb. 6, 1945, with the chief complaints of abdominal pain, vomiting, and the passage of tarry stools.

Since the age of 1 year the patient had numerous episodes of vomiting, often of such severity that his face became livid. During these attacks the infant doubled up, apparently from pain. At the age of 5 years it became established that the pain occurred in the epigastrium and right upper quadrant. It came in waves with peaks of intensity and intervening periods of relief lasting several minutes. These attacks occurred at any time, sometimes while the patient was eating, sometimes several hours after a meal, and occasionally at night. The vomitus contained recently ingested food and was seldom large in quantity. Recovery from these episodes was always prompt and the appetite remained good. This syndrome was diagnosed as appendicitis several times. On one occasion, when the boy was 9 years of age, elective appendectomy was prevented only by the sudden development of scarlet fever.

Two weeks before admission to the hospital the boy began to experience the pain and vomiting several times daily. These attacks were unrelieved by powders prescribed by the physician. The mother noticed two days prior to admission that the boy was passing tarry stools. On questioning, he stated that the stools had been dark for several days.

There were no symptoms referable to other systems and the past medical and family histories were noncontributory.

**Physical Examination.**—The patient was moderately obese, very pale, and apprehensive. The temperature was 100° F.; pulse, 120; respiration, 20; and blood pressure,

100/50. Except for paleness of the conjunctive as well as other mucous membranes, and a soft systolic mitral murmur, the physical examination was negative. Repeated abdominal examinations revealed no mass or other abnormality.

*Laboratory Studies*.—Blood count revealed: hemoglobin, 38 per cent; red blood cells, 2,400,000, color index, 0.80; white blood cells, 4,500, differential count, normal. Two per cent of the red blood cells were normoblasts and the platelets numbered 390,000. Tests of hemostatic function were normal. Repeated urinalyses were negative. Blood Wassermann and Kahn reactions likewise were negative. Stool examinations, with the patient receiving a meat free diet, revealed strongly positive benzidine reactions.

The prothrombin time was 100 per cent of average normal; bromsulphalein liver function test revealed 3 per cent dye retention, and the serum bilirubin was 0.4 milligram. Blood culture was negative.

Röntgenologic study of the upper gastrointestinal tract with barium by Dr. Paul C. Swenson revealed the following. The esophagus and stomach were essentially normal, except for considerable pylorospasm early in the examination. This later relaxed and a normal duodenal bulb was visualized. In the second portion of the duodenum there was found an elongated filling defect which forced the barium to the periphery (Figs. 1 and 2). There was a slight irregularity at the distal portion of the defect suggestive of ulceration. The remainder of the upper small bowel was normal. There was no evidence of gastric retention at the end of six hours. These findings were interpreted as suggestive of leiomyoma in the second portion of the duodenum with ulceration.



Fig. 1.—Preoperative gastrointestinal series, showing filling defect in second portion of duodenum.

*Subsequent Course*.—The patient remained in the hospital twenty days, during which time he remained asymptomatic. He received three blood transfusions of 500 c.c. each on Feb. 5, 8, and 14. At the time of discharge on Feb. 24, 1945, the hemoglobin was 80 per cent, red blood cell count 4,100,000, and benzidine test of the stool negative. The boy's parents elected to take him home for several weeks, to return then as a private patient when the surgeon of their choice would be available.

*Second Hospital Admission.*—The patient was readmitted on April 13, 1945, to the private surgical service. He had remained asymptomatic in the interim. Blood count revealed a hemoglobin of 82 per cent and red blood cell count of 4,120,000. Repeat roentgenologic examination of the duodenum revealed the same defect at the bottom of the U loop. At this time there was no evidence of ulceration.

The preoperative diagnosis was leiomyoma of the duodenum or gastric polyp prolapsed into the duodenum.

*Operation.*—On April 16, 1945, under ether anesthesia, the abdomen was opened through a right upper rectus muscle-splitting incision. The duodenum appeared normal in size, but palpation revealed a semispherical mass about 3 cm. in diameter in the second portion along the mesenteric border adjacent to the pancreas. In order to rule out a prolapsed gastric polyp, a gastrotomy incision was made anteriorly in the prepyloric region. A finger was introduced into the lumen of the stomach. No polyp or other abnormality was noted, so the finger was advanced through the pylorus into the duodenum. Along the posterior wall of the second portion there was felt a smooth, circumscribed, semispherical mass, apparently arising



FIG. 2.—Spot pressure film of filling defect shown in FIG. 1.

within the wall of the duodenum and projecting well into the lumen. A longitudinal incision about 5 cm. long was made into the lumen of the duodenum through the anterior wall opposite the mass. The ampulla of Vater was located about 2 cm. above the upper limit of the mass. Immediately adjacent to the upper border of the mass the lumen of another duct presented. A fine blunt probe was inserted and passed obliquely upward readily for a distance of approximately 3 cm. into the pancreas. It had no demonstrable communication with the adjacent mass. From within the duodenum a transverse incision was made through the mucosa overlying the mass. With moderate difficulty the mass, which occupied a submucous position, was excised intact without rupturing through the posterior duodenal wall. The mucosal incision as well as the longitudinal one through the anterior wall were closed, thus re-establishing the continuity of the duodenum. Following closure of the gastrotomy incision the abdomen was sutured in layers without drainage.

The patient received 500 c.c. of blood during the operation and remained in good condition throughout. Total operating time was one hour and thirty minutes.

*Pathologic Examination.*—The specimen consisted of a thin walled cyst measuring 2.3 by 2.1 by 1.5 centimeters. Slightly more than half of the external surface was rounded, smooth, and glistening, whereas the remainder was somewhat flattened, rough, and shaggy (Fig. 3). The lumen contained thick cloudy fluid.

Histologic examination revealed that the cyst was lined by a duodenal type of mucosa. The outer wall consisted of muscularis (Fig. 4).



Fig. 3—Photograph of gross specimen.

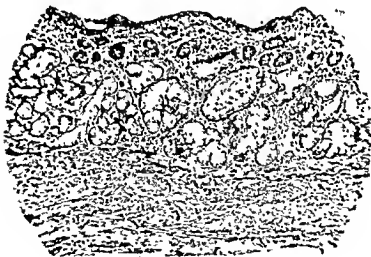


Fig. 4—Photomicrograph (X100) of cyst wall, showing duodenal type of mucosa and well-developed muscularis.

*Postoperative Course*—Wangenstein suction and parenteral feeding were instituted for six days postoperatively. The wound healed primarily and the entire convalescence was uneventful. At no time did the temperature postoperatively rise above 100° Fahrenheit. The patient was discharged in good condition on May 5, 1945, the nineteenth postoperative day.

*Follow up*—Four months postoperatively the boy was free of pain, vomiting, and tarry stools. The wound was well healed and the patient had gained 12 pounds. Re-examination of the upper gastrointestinal tract at this time showed free egress of the barium through the pylorus and duodenum, the smooth surface in the mucosal pattern apparently being normal in the region previously shown to have extraluminal pressure (Fig 5).

One year following operation the patient was entirely well.



Fig 5—Postoperative gastrointestinal series showing normal contour in second portion of duodenum.

#### DISCUSSION

The rarity of enterogenous cysts of the duodenum is demonstrated by the fact that we have been able to collect only thirteen previously reported cases from the world literature. These include seven cases from the excellent previous review by Gardner and Hart,<sup>1</sup> one<sup>2</sup> from the German literature not included by these authors, and five<sup>3-7</sup> reported since their article. Our case brings the total to fourteen (Table I).

Of the total cases, ten were encountered between birth and the age of four months. The oldest patient was 15 years of age. The average age for the group was 3 years. Three patients were males, nine were females, and the sex of the remaining two was not mentioned. None were reported in the colored race.

TABLE I ANALYSIS OF CASES

CASE	AUTHORS	YEAR	AGE, SEX, AND COLOR	QUANTITATIVE SYMPTOMS	WEIGHT IN G	PERFORATIVE DIAGNOSIS	TREATMENT	RESULT
1	Sanger and Kleph <sup>14</sup>	1880	Birth, M, W	-	-	-	None	Died at birth
2	Roth <sup>15</sup>	1881	Birth, M, W	-	+	-	None	Died at birth
3	Meyer <sup>16</sup>	1919	3 yr, F, W	+	-	Pylorospasm	None	Died
4	Wauha <sup>17</sup>	1923	10 days, F, W	+	+	Duodenal obstruction from abdominal tumor	First, cyst opened and packed with gauze, second, cyst marsupialized	Refilled in eight weeks Died six days postoperatively
5	Maddox <sup>18</sup>	1927	3 mo, F, W	+	+	-	Exploratory laparotomy	Died sixteen hours postoperatively
6	Sohn <sup>19</sup>	1927	8 yr, F, W	+	+	Intussusception	Resection of pylorus and first part of duodenum	Well
7	Smith <sup>20</sup>	1930	2 wk, F, W	+	+	Pyloric stenosis	Cyst drained externally	Died one week postoperatively
8	Gardner and Hart <sup>21</sup>	1935	15 yr, F, W	+	+	Cholelithus cyst	Widened anastomosis of cyst and duodenum	Well
9	Ladd <sup>22</sup>	1937	5 wk, F, W	+	+	Mesenteric, omental, or enteric cyst	Resection of cyst and first part of duodenum. posterior gastroduodenostomy	Well
10	Barnes <sup>23</sup>	1938	4 wk, F, W	+	+	Hypertrophic pyloric stenosis	First, cyst aspirated, second, seventh day, posterior gas trojejunostomy	Well
11	Puchman <sup>24</sup>	1939	4 mo, F, W	+	+	Cyst of the abdomen	Prophy of cyst wall; catheter drainage	Died four hours postoperatively
12	Gillespie and Rogers <sup>25</sup>	1940	4½ yr, F, W	+	+	-	Excision of tumor, closure of duodenum, T tube drainage of common bile duct	Well
13	Organs <sup>27</sup>	1943	4 wk, F, W	+	+	Mesenteric cyst causing pyloric obstruction	Resection of part of stomach and duodenum, with end-to-end anastomosis	Well
14	Authors' case	1945	12 yr, M, W	+	-	Leiomyoma of duodenum	Excision of cyst from within duodenal lumen	Well



Although the exact etiology of this condition has not been definitely established, authors agree that it is the result of a developmental defect. Lewis and Thyng<sup>8</sup> observed knoblike diverticula along the entire intestinal tract of embryos of man, the pig, and the rabbit. Though the earliest of these appeared in the region of the duodenum, the greater number subsequently appeared along the terminal ileum. Most of them degenerated. The detachment of one might account for the development of an enterogenous cyst. In support of these authors' theory is the fact that the enterogenous cysts are by far most frequent in the region of the terminal ileum, corresponding to the area in which the fetal diverticula were most frequently noted.

Hughes-Jones<sup>9</sup> demonstrated in human embryos the presence of islands of epithelial tissue like that of the intestine lying close to but not in the intestinal wall. It is thus possible that sequestration of embryonal intestinal epithelium early in fetal life may give rise to enterogenous cysts.

Maddox<sup>10</sup> favors the theory of origin from a vacuole, arising during the so-called solid stage of the intestine, which fails to gain communication with the developing lumen. Fusion of several such isolated vacuoles might also explain the development of the long tubular structures which course through the mesentery alongside of the gut and to which the term "duplications of the alimentary tract" has been applied. Ladd and Gross<sup>11</sup> emphasize that enterogenous cysts originate from the same kind of developmental aberration as these elongated hollow structures and prefer the all-inclusive name of "duplications of the alimentary tract" for both lesions.

In spite of the seemingly wide pathologic variations, these cysts possess three fundamental features. They are intimately adherent to some portion of the duodenum, they are cystic, containing fluid; and their walls are composed of all layers of the intestine.

In the present series there were two cases in which enterogenous cysts were present also in other portions of the alimentary tract. Five were attached to the first portion of the duodenum and five to the second portion. In four cases the exact location was not stated. The cysts were usually round or pear shaped. One was reported as pedunculated (Case 2). The size varied from 2 to 12 cm in diameter. The largest contained 550 c.c. of fluid. Usually the fluid is clear, pale, and mucoid, representing the secretion of its own epithelial lining. Occasionally, when high intra-cystic pressure causes degeneration or necrosis of the lining membrane, the fluid may be cloudy or dark due to hemorrhage (Case 11). In no case was a communication with the lumen of the duodenum reported.

Multiple congenital abnormalities were noted in several instances. Case 1 exhibited multiple cysts of the intestine and biliary passages, several accessory spleens, and complete transposition of the viscera. In Case 2, similar cysts of the terminal ileum and posterior mediastinum were reported. Blind ending of the pancreatic duct in the cyst wall was described in Case 5. In our case the duct which emptied into the duodenum 2 cm. below the ampulla of Vater and adjacent to the cyst is regarded as one of the variant positions of the accessory pancreatic duct diagrammed by Schmieden and Sebening.<sup>12</sup>

Histologic examination of the cyst wall reveals a mucosal lining which is usually duodenal in type. Occasionally, because of pressure necrosis, this lining may be partially or wholly denuded, covered by a fibrinous exudate, and the submucosa may contain small groups of mucous glands and lymphoid nodules (Case 9). It is probable that the mucosal lining may at times correspond to that at other levels in the gastrointestinal tract, since this feature has been observed in enterogenous cysts elsewhere.

The presence of a smooth muscle coat is an important constant feature of the lesion. This muscularis may be thin and attenuated (Case 5) or may be thick and well differentiated into an outer longitudinal and inner circular layer (Case 11). It is adherent to or continuous with the muscularis of the duodenum, allowing no plane of cleavage.

The duodenum does not represent the most frequent site for occurrence of these cysts. Of 102 reported cases collected by Hudson,<sup>12</sup> only eight were in the duodenum. Although they may occur at any level of the alimentary tract from the base of the tongue to the anus, they are by far most frequent in the ileocecal region (65 per cent of the fifty-five reported by Hughes-Jones<sup>9</sup>).

Encroachment upon the duodenal lumen by the intramural lesion produces obstructive symptoms. Intermittent colicky pain was a prominent symptom in our case as well as in two of the other three older patients. It was not mentioned in those reports dealing with infants. Vomiting was a constant symptom except in those patients who died at birth. The vomitus may or may not contain bile depending upon the location of the lesion with respect to the ampulla of Vater. Visible peristalsis may be observed across the upper abdominal wall and there may be some fullness in the same area. A mass was palpable in all but three cases. Melena was reported in four cases and was associated with hematemesis in one. In our case a profound anemia was produced. The bleeding occurs from ulceration of the overlying duodenal mucosa, probably due to pressure necrosis. Jaundice was present in one case, resulting from extrinsic pressure on the common bile duct. Plain roentgenogram of the abdomen may show a soft tissue mass in the right upper quadrant. Upper gastrointestinal study with barium frequently reveals duodenal obstruction and gastric retention of barium after six hours. In our case an irregularity of the filling defect suggested ulceration. Barium enema may show displacement of a portion of the colon. Intravenous pyelography may be of aid in excluding a renal tumor.

The lesion has never been specifically diagnosed preoperatively and has seldom even been considered as a diagnostic possibility. Fluctuant masses would necessitate differential exclusion of other cysts, namely, omental, chylous, dermoid, pancreatic, and choledochal. More resistant masses may resemble hypertrophic pyloric stenosis, intussusception, renal tumor, or leiomyoma. In the absence of any mass, pylorospasm and congenital duodenal diverticulum, atresia, or bands must be considered.

Treatment of these lesions is surgical. The method employed must be adapted to the individual case, being largely determined by the size and position of the cyst and by the age and condition of the patient. The ideal procedure, excision of the cyst, is usually mechanically impractical because of continuity

of the muscle layers of the cyst and duodenum. In addition, it is dangerous because the cyst and adjacent duodenum have a common blood supply. Injury to these vessels during excision of the cyst might lead to gangrene of the bowel wall. That such a procedure may be employed with success in some instances is illustrated by our case in which the cyst was excised from within the duodenal lumen and by the case of Gillespie and Rogers<sup>2</sup> in which it was excised from without.

Resection of that part of the duodenum bearing the cyst followed by re-establishment of continuity of the gastrointestinal tract provides complete cure (cases of Orgias<sup>7</sup> and Sohn<sup>2</sup>) but is not feasible when this would involve the pancreatic and biliary ducts. It is a formidable procedure in an infant or debilitated child. In such poor risk cases internal drainage may be provided by window anastomosis of the cyst to the adjacent duodenal lumen, as successfully performed by Gardner and Hart.<sup>4</sup> These same authors have suggested a more complicated form of internal drainage by anastomosis of the cyst to a loop of jejunum, the segments of which are united by a jejunojejunostomy. The fecal stream is thus diverted from the cyst.

Although not a method of choice, marsupialization of the cyst, particularly if large, could be undertaken if other procedures appeared unduly hazardous. Aspiration or catheter drainage are mentioned only to be condemned. Relief of obstruction by gastroenterostomy, without carrying out any procedure on the cyst itself, was successfully employed in one case.

Accurate evaluation of the over-all mortality (50 per cent), as well as the merits of the various operative procedures, is impossible due to the small number of cases. However, it is apparent that the high mortality is due to the extremely early age of the average cases and the frequently poor preoperative condition of these infants. Of the ten patients whose ages ranged from birth to four months, three died at birth or shortly thereafter and only three of the remaining seven recovered following operative procedures. On the other hand, all four of the older patients recovered following surgical treatment.

The immediate and ultimate prognosis in the older age patients is apparently good. The high mortality to date in the infant group may perhaps be reduced in the future by stricter attention to pre- and postoperative care in co-operation with a competent pediatrician.

#### SUMMARY AND CONCLUSIONS

1 Enterogenous cysts of the duodenum are exceedingly rare. We are reporting the fourteenth case.

2. These congenital cysts originate as developmental defects. They contain all the coats of the bowel and their muscularis is continuous with that of the duodenum.

3 The diagnosis should be considered when an infant or child presents symptoms of duodenal obstruction. A mass may be palpable in the upper abdomen, and occasionally melena may be noted. Roentgen-ray examination may be a valuable diagnostic aid.

4. Simple excision, though rarely possible because of continuity of the muscle layers, was successfully performed in our case. Excision of the cyst usually requires resection of that portion of the duodenum bearing it. If the patient's condition or the location of the lesion do not permit resection, internal drainage or gastrojejunostomy are advocated. Results of external drainage are poor.

5. Proper choice of operative procedure for the individual case coupled with meticulous pre- and postoperative care may lower the high mortality in the infant group. The prognosis is excellent in older patients.

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## INTRAPERITONEAL HEMORRHAGE COMPLICATING SIMPLE LARGE BOWEL OBSTRUCTION

FRANK N. DEALY, M.D.,\* AND PETER A. MICELI, M.D.†  
JAMAICA, N. Y.

THE effects of bowel distention, both in experimental animals and clinical cases, have been the subject of extensive study during the past twenty-five years. As a result, fanciful theories on the nature of the "absorbed toxins" have been replaced gradually by logical, mechanical concepts. To Owen H. Wangensteen goes much of the credit for the emphasis on the mechanical aspects of bowel obstruction.

It has been our experience to encounter an effect of distention hitherto unreported in the literature. This complicating factor is intraperitoneal hemorrhage arising from a subserosal vein and is self-limited in extent. We report herein two cases of large bowel obstruction of the closed loop variety. The intraperitoneal hemorrhage arose, in each case, from the anterior cecal vein which crosses the cecum at right angles to the long axis of the bowel, at or near the level of the ileocecal junction.

### CASE REPORTS

**CASE 1 (A 61041)**—E. B., a 79 year old white woman, was admitted to the surgical service of the Queens General Hospital on March 18, 1943, complaining of lower abdominal pain. The pain had been colicky in nature and located in the umbilical region at its onset thirty-six hours before. Ten hours after the pain began the patient vomited food particles. She vomited several times thereafter and noted brownish, "bad smelling" vomitus. She passed no stools after the illness began but continued to pass some flatus.

**Past History**—During the preceding three years the patient had lost 35 pounds in weight. The stools had always been well formed and regular up to the present illness. Six months before admission she noted occasional bright red blood in the stools. For thirty years the uterus had been prolapsed but caused the patient no particular inconvenience.

**Physical Examination**—The patient was emaciated, elderly, and of small stature, and appeared to be in moderate distress. History taking proved to be difficult because of her poor hearing, but she was well oriented and alert. The temperature was 100° F., pulse 84, and blood pressure 130/70. The tongue was coated white and the breath was fetid. The heart was not enlarged, and the rhythm was the regular sinus type. No murmurs were detected. The lungs were similarly devoid of pathology. The abdomen was slightly distended. Spasm of the recti muscles was present in moderate degree. Tenderness was diffuse but most intense in the right lower quadrant. A vague impression of a mass in the right lower quadrant was masked by muscle spasm. The rebound phenomenon was most notable in the same area. Auscultation failed to reveal any borborygmi and a "silent" abdomen was diagnosed.

Rectal examination added no further information.

Vaginal examination confirmed the presence of a complete uterine procidentia with marked erosion of the cervix.

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\*Director of Surgery, Queens General Hospital.

†Assistant Visiting Surgeon, Queens General Hospital.

*Laboratory Data.*—Tests revealed: white blood cells, 18,500, polymorphonuclears, 80 per cent; red blood cells, 3,800,000; hemoglobin, 65 per cent

Urinalysis revealed no abnormal elements.

*Working Diagnoses.*—Diagnoses were: (1) acute appendicitis with perforation, (2) aeoplasm of the colon with perforation; and (3) diverticulitis with perforation.

*Course.*—The patient was placed on Ochsner regime with Wangenstein suction via duodenal tube. Fluids and electrolytes were restored. After ten hours of such therapy and observation further delay was considered dangerous and the condition optimal. At this time signs of pathology were well localized to the right lower quadrant.

*Operation.*—Anesthesia consisted of 1 per cent procaine field block supplemented in the later stages by cyclopropane. The abdomen was entered via a McBurney incision. Upon opening the peritoneum bloody fluid gushed out. After suctioning, the cecum was found to be much distended and its anterior surface hematomatous. The cecal serosa was split in the long axis of the bowel, close to the anterior longitudinal band. The edges of the split serosa were approximately 2 cm apart. Palpation of the ascending colon revealed an annular obstructing carcinoma at the level of the hepatic flexure. The appendix was normal. A clamp cecostomy was performed and the wound was closed in layers about the exteriorized bowel. Postoperatively, Wangenstein suction was continued. On the third day the clamp came loose with subsequent outpouring of gas and feces. Thereafter drainage was profuse and uninterrupted. The patient was gotten out of bed early and frequently. There were no postoperative complications.

On April 9, 1943, she was reoperated upon. Obstructive resection of the hepatic flexure was performed using intercostal block anesthesia. She was permitted out of bed on the first postoperative day and daily thereafter. Spur crushing was begun two weeks later. On June 11, 1943, colostomy closure was performed. Stools were passed rectally after the third postoperative day. The cecostomy failed to close spontaneously, necessitating surgical closure. The patient left the hospital on Aug. 22, 1943, and is now living in a home for the aged. Microscopic report on the resected tumor was adenocarcinoma grade 2 C.

**CASE 2 (A 6341).**—C. M., a 59 year old white man, entered Queens General Hospital on Jan. 21, 1940, complaining of pain in the abdomen of twenty-four hours' duration. Ten days before admission he had a bout of colicky pain which lasted one and one half days and which he attributed to the eating of "hot dogs." There was no nausea or vomiting. Self treatment with "salts" resulted in several bowel movements and relief from pain. There were no further symptoms until the night before admission, when sharp epigastric pains began and were followed shortly by vomiting. After several hours the epigastric pains subsided but a residual soreness was noted in the right lower quadrant. The patient noted a "blown up" appearance in that area. The soreness persisted there causing him to seek relief by the taking of salts. A normal bowel movement resulted after several hours.

*Past History.*—Iridectomy was done thirty five years before for sequela of trauma. Three years prior to this illness hematemesis occurred and the patient entered a neighboring hospital. He requested his release before a diagnosis could be established. There was no recurrence of bleeding, no weight loss, and no further stomach trouble since that time. He reported daily and copious drinking of beer and whisky.

A mild degree of constipation during the preceding year had been amenable to mild cathartics.

*Physical Examination.*—The patient was a well nourished and well developed white man of stated age who appeared to be in slight distress. Temperature was 99.6° F., pulse 100 and respirations 16. The right eye was marked by an old iridectomy scar. The chest was emphysematous in type, but no pulmonary pathology was demonstrable. The heart was not enlarged and no murmurs were heard. The rhythm was regular and slightly rapid. The abdomen was diffusely tender with greatest sensitivity found over McBurney's point. A definite prominence in the right lower quadrant was partly masked by rigidity of the right rectus muscle. This mass was thought to be cecum.

*Laboratory Data.*—Tests revealed: white blood cells, 14,000; polymorphonuclears, 89 per cent, red blood cells, 4,110,000; hemoglobin, 110 per cent.

The urine was unaltered.

*Working Diagnoses.*—Diagnoses were: (1) appendiceal abscess and (2) carcinoma of the colon

*Operation.*—The operation was performed under spinal anesthesia, using 150 mg novocain. The abdomen was entered through a McBurney incision. The cecum and transverse colon were found markedly distended. A large amount of frankly bloody fluid was found in the general peritoneal cavity. The serosa of the cecum was split in the long axis of the bowel and subserosal hematoma was noted.

A second incision, a right recto-, was made. Further exploration revealed an annular obstructing carcinoma of the transverse colon close to the splenic flexure. Clamp cecostomy was performed inasmuch as distension precluded resection and end to end anastomosis.

Subsequently, the tumor bearing bowel was resected at another operation and end to end anastomosis performed. The cecostomy was closed later. This patient returned after two years with recurrence of obstruction. Diffuse metastatic carcinoma was discovered at laparotomy. He died in 1943. Microscopic report on the resected tumor was adenocarcinoma grade 1 2 B.

#### DISCUSSION

An explanation for the site of hemorrhage is obtained in part from Wangensteen's formula<sup>1</sup> for tension in a hollow viscus,  $T = \pi DP$ ; or the tension (stretch) on each centimeter of bowel wall equals the product of pi (3.14), the diameter of the bowel, and the intraluminal pressure. In this way it is shown that the cecum is subjected to the greatest stress in closed loops, because its diameter is greatest. However, the thickness and elasticity of the bowel wall are also factors which must be considered. The cecum is an elastic, peristaltic organ which at some point becomes fatigued and then overstretched beyond its normal limit of elasticity. Further complication arises from the difference in elasticity of the various layers of the bowel wall.

Clinically, gangrene and perforation of the cecum have been noted many times in cases of obstructing carcinomas of the large bowel distal to the cecum. Before gangrene and perforation occur, it is reasonable to assume, and has been noted experimentally and clinically, that the serosa splits. Thus, its action as a limiting membrane is lost and the mucosa, which is relatively more elastic, distends further. The blood vessels which course through the subserosal tissues, particularly the veins, are stretched beyond their limit of elasticity and consequently rupture.

Age, with accompanying sclerosis, is a probable predisposing factor. With the rupture of the vessel, hemorrhage occurs into the subserosal tissues and, by direct extension, into the peritoneal cavity. Bleeding is self-limited due to retraction of the vessel.

With the onset of hemorrhage into the general peritoneal cavity, the patient presents an acute abdominal syndrome. The findings of muscle spasm and excessive tenderness with rebound phenomenon are not the usual signs of simple obstruction. Gangrene of the bowel and perforation of the cecum or of carcinoma elsewhere are to be considered more logically. The hematomatous cecum gives rise to such well-localized tenderness that appendicitis will inevitably be considered in the diagnosis. When operation is performed copious bloody fluid

will be found in the peritoneal cavity, sometimes in sufficient amount as to pour out on incision of the peritoneum. Further examination then reveals the cecal vessel as the site of hemorrhage and the presence of obstruction in the ascending, transverse, or descending colons.

Review of the literature for the past thirty years failed to uncover any reports of similar cases. This pathology is not included among the effects of distention by Wangenstein.<sup>1</sup> Dr Wangenstein states<sup>2</sup> that he has never seen this entity. We feel that cause and effect are fairly well linked in both cases reported and that the mechanism postulated is a logical one. We believe, too, that it is related to abdominal apoplexies<sup>3</sup> in that sclerotic changes are predisposing factors. The exciting factor is, of course, the distention consequent to organic obstruction.

The awareness on the part of surgeons as to this possible complication of large bowel obstruction, particularly in older age groups, may lead to better diagnosis and avoidance of improper incisions, poorly timed operations, and unnecessary morbidity.

#### CONCLUSION

Two cases of large bowel obstruction with marked distension of the cecum are presented, which apparently have led to stretching of the anterior cecal vein with regional hematoma and intraperitoneal hemorrhage. The theoretical bases for this lesion is discussed. No previous complication of this nature was found in the literature.

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## TANTALUM CRANIOPLASTY, A METHOD FOR ONE-PIECE FIXATION

MAJOR HENRY C. DAILEEN, MEDICAL CORPS, ARMY OF THE UNITED STATES

**T**ANTALUM used as the "graft" in cranioplastic procedures has definite advantages over any material previously employed. Since it has been used with increasing frequency and seems to enjoy only favorable reports, I consider it worth while to describe a new method of fixation which is suitable for use with this metal, simple to accomplish, and definitive.

### INDICATIONS FOR CRANIOPLASTY

The indications for cranioplasty are well agreed upon by neurosurgeons in this country. Grant and Norcross<sup>1</sup> listed them as follows:

1. Severe headache and other symptoms of the trephined; dizziness, undue fatigability, vague discomfort at the site of the defect, a feeling of apprehension and insecurity, mental depression, and intolerance to vibration.
2. Epilepsy, when the attacks originated from the injury that caused the defect.
3. Those cases in which there is danger of trauma at the site of the defect.
4. Cases that have unsightly defects.
5. Defects that pulsate unduly or that are painful.

Mayfield and Levitch<sup>2</sup> were not impressed by any relief from epilepsy following the repair of the cranial defects but remained in exact accord as to the other indications.

In the absence of contraindications which are well defined as (1) infection, (2) foreign body, (3) increased cerebrospinal fluid pressure, (4) pathologic cerebrospinal fluid changes, (5) further intracranial surgery planned through the same approach, and (6) a systemic condition contraindicating any surgery, I feel that there should be only one indication for cranioplasty, namely, *a defect in the skull*. Of course, this dogmatic statement is to be modified as individual cases merit. Generally, those defects less than 2.5 cm. in diameter need not be closed since their effect on the brain is negligible. In 1932, Reed<sup>3</sup> first suggested this sole indication for cranioplasty when he said, "The operation is so safe, so easy to perform, and in most cases gives such satisfactory results that every adult patient with such a defect should be given the benefit of a plastic repair." Since he expressed this opinion tantalum has made the operation even simpler and safer. In his article he described a patient with severe Jacksonian seizures who was markedly relieved by a bone graft done after the method of Frazier. Since he had never observed such results in prior surgery, and since in this patient's very large defect, movement and bulging of the brain were apparent, he surmised, "... the stopping of the attacks following the stabilizing of the brain within the skull by closing the defect makes me feel that the cause of the attack may be due more to motions of the brain from this instability

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than to adhesions between the brain and dura." This opinion agrees wholeheartedly with that of Gardner<sup>4,5</sup> who pleaded for early closure of all skull defects.

The brain is normally a nonpulsating organ and when significant sized defects in the skull exist it is transformed into a pulsating mass which leads to definite pathologic changes in the brain tissue near the defect. Whether these changes, which may be as marked as the formation of definite cerebral cysts, are due to pulsation, herniation, or change of circulatory characteristics need not be argued. The conclusion remains to avoid these abnormal reactions, all skull defects should be closed as early as possible.

## THE CHOICE OF A BONE SUBSTITUTE

A substance used to replace bone in skull defects, and the procedure used to implant it, should have the following characteristics

- 1 Material readily available
- 2 Material easily molded into intricate contours when needed, either by the cast and die method or by shaping at the operating table
- 3 Material of similar rigidity, strength and protection to the bone which it replaces
- 4 No special tools required to cut or trim at the operating table
- 5 Procedure easy, uncomplicated, and fast
- 6 Lack of any reaction between the substance used and the body tissues
- 7 Immobility after insertion
- 8 No uncomfortable side-effects on the patient, that is, heat or cold absorption, too weighty, etc

That tantalum fits these requirements has been shown by many past studies, as those of Pudenz<sup>6</sup> and others. He has shown that there is almost no foreign body reaction even when tantalum is placed within the substance of the brain, it produces much less reaction than other foreign substances used in neurosurgery, the encapsulation which does occur is minimal and nonprogressive, and normal regeneration of bone in the vicinity of the plate is not impaired. Many authors have pointed to the ease with which tantalum is used in surgery.

## NEED FOR FIXATION

It is generally agreed that plates which depend solely on the overlying galea and skin for fixation are likely to slip out of place, sometimes to a marked degree. Gardner<sup>7</sup> reported two such cases which required reoperation and one instance in which even wire sutures snapped and allowed the plate to wander. The possibility of elevation by the accumulation of fluid below the plate is ever present and for this reason alone some form of fastening of the metal to the skull should be used. Various methods which have been reported for fixation of metal to the cranium are shown diagrammatically in Fig. 1. Since an elevation of 0.015 inches cannot be palpated below the scalp, I think it unnecessary to spend the time at the operating table fashioning a ledge around the entire circumference of a defect in order that the plate will lie flush with the bone.

This can only cause unneeded trauma and prolonged anesthesia. The use of screws to fix the plate is a popular procedure. At the present time tantalum screws are not available and the use of vitallium screws, as suggested by some, is to be condemned because of its electrolytic effects when placed in contact with the tantalum plate. Army neurosurgeons at two large neurosurgical centers are using tantalum wedges driven into the skull in the same fashion that a pane of glass is held in its frame with glazier's points.<sup>8</sup> These wedges either may

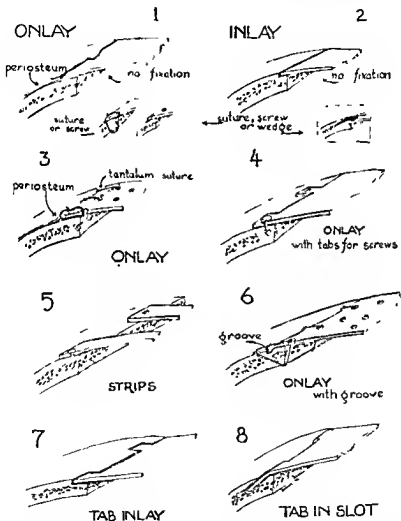


Fig 1—Various published methods of using and attaching metal to the skull. 1, Without fixation, or with wire sutures or screws. 2, no fixation, or fixed by "springing" plate into the ledge "A-B" or by using glazier's points (inset),<sup>8</sup> these also may be inserted through slots cut near the margin of the plate. 3, onlay with pericranium over edge of plate.<sup>10</sup> 4, onlay with projecting tabs for screws.<sup>11</sup> 5, onlay strips with screws.<sup>12</sup> 6, onlay with plate edges buried in groove.<sup>13</sup> 7, tabs inlay into skull with outline of plate fitting loosely within defect.<sup>14</sup> 8, method proposed in this paper.



## APPLICATION OF THE PLATE TO THE DEFECT

The patient is placed on the operating table with the head on a rest which will allow unobstructed use of the operator's hands in all directions. The operative field is prepared and draped in the usual manner. This should include a prior complete head shave and the drapes sutured in place. The incision employed varies with the size and position of the defect. In any case, the pericranium is exposed and the galea reflected back from the edges of the defect for as little a distance as possible compatible with good exposure. The periosteum is incised around the borders of the defect and reflected peripherally for a distance of 1 cm. I have not considered it necessary to remove



Fig. 2.—Skull prepared to receive plate. Arrows indicate slots in outer table of skull. Note the tabs on the tantalum plate. This plate pre-form-1.

the scar tissue which is always found filling an old defect. Removal can only cause considerable irritation and stimulation to further growth of the scar. The scar will not continue to proliferate under the nonreactive tantalum plate and its presence serves to fill the dead space which would otherwise remain between the dura and the metal. This view is contrary to the published procedures of most neurosurgeons but it is supported by the experiences of Adson<sup>11</sup> who places many of his plates just beneath the galea without disturbing the periosteum or the underlying scar. He points out that only where signs of cerebral irritation exist is it necessary to resect the meningeal scar tissue and, if needed, the cerebral scar. Next, the plate is placed over the defect and any minor alterations on the plate may be made at this time. The positions of the

tabs are marked on the skull by placing the tip of a small nail drill (as is manufactured for releasing subungual hemorrhage) in the indentations at the base angles of the tabs. In this way two marks are made on the skull to indicate the extent and exact position of each tab base.

A slot is then cut tangentially into the skull from one base mark to the other. This slot is directed at a very wide angle into the skull so that the tips of the tabs will lie in the diploë space. One must be cautious in drilling that the inner table of the skull is not perforated.

The slots are easily formed by using a small twist drill to drill three holes into the skull for the required distance. A small dental chisel is then used to remove the partitions between the holes. This method was used in two of my cases (Fig 2). No special tools are needed for this procedure, but it requires a few minutes more to do than when the slots are cut with a dental engine and hand piece. The latter method has proved very satisfactory and two standard dental burs are necessary. The initial drilling is done with a No. 2 burr which bores a tubular opening to the necessary depth. Into this opening a No. 557 burr is inserted. This instrument has a side cutting surface 5 mm. long and can cut laterally in the skull easily with gentle pressure. By sliding this burr in and out while cutting, one can cut slots to a depth of 1 cm. easily. When this method is used, slots are cut narrower and more perfectly than by the drill and chisel. One must be careful that the side-cutting burr does not "wander" when directing it laterally.

If these slots are placed carefully, the tabs on the tantalum plate will fit into them perfectly. The last tab is inserted into its slot by "springing" the plate enough to allow the tip to enter the slot. When the plate snaps back it will be found to lie in close approximation to the skull around its entire circumference and it will be fixed firmly in place against movement in any direction. A plate anchored in this way is seen in Fig 3. Considerable pressure is needed to elevate a plate fixed to the skull in this manner.

Absolute hemostasis is extremely important prior to replacing the scalp flap since accumulation of serum and blood is very prone to occur over the metal plate. The galea and skin are closed in layers by interrupted silk sutures.

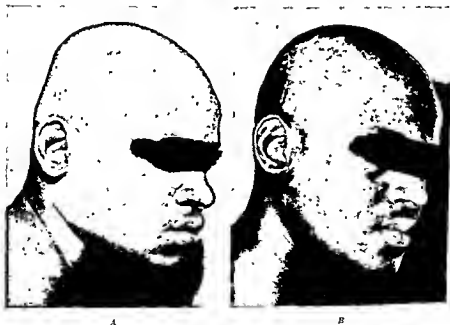
#### CASE REPORTS

**CASE 1**—A 21-year-old colored laborer was admitted to the Oak Ridge Hospital June 14, 1945, with an extensive left temporal laceration (Fig 4A and B). This was treated and the patient sent to bed for observation. A large protuberance had been noted in the right occipital area. It was hard, fixed, and nontender and had been present five years. Since it was located just where a hat brim would strike and had caused the patient a moderate amount of distress, he expressed a desire to have it removed. General, neurologic, fundoscopic, visual field, and laboratory examinations were normal. Roentgenogram revealed a large bone tumor of the right occipitoparietal area.

This tumor was removed at operation June 27, 1945. Six months later a pre-formed tantalum plate was placed over the defect by the tab-in-slot method. In spite of meticulous hemostasis there was a marked formation of fluid and collection of dark blood under the flap which required daily postoperative aspirations for two weeks. This ceased abruptly in the third week and the wound required no care after that.



Fig 3—Tantalum plate in place. Kocher clamps indicate fixation points.



A

B

Fig 4—Pre- and postoperative appearance of skull defect. A, preoperative, B, postoperative

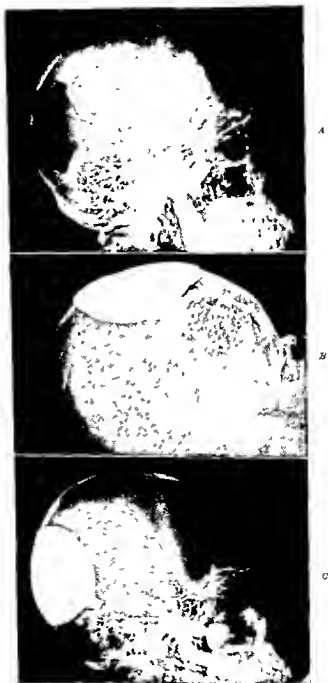


Fig 5—Appearance of skull by x-ray before and after plating. A, Preplating defect; B, tangential view of plate in place note close approximation at plate edges. C, lateral view of skull with plate in place.



The patient works in the Oak Ridge Hospital and daily cursory examinations have been possible. The plate remains solidly anchored in place and the scalp stays firmly against it. The patient is not aware of the presence of the plate, and he has no complaints referable to the operation (Fig 5A, B, and C).

**CASE 2**—A 46 year old millwright was seen at the Oak Ridge Hospital Aug 27, 1945, with a severe, depressed, compound, comminuted skull fracture just to the right of the mid-sagittal line in the mid parietal region (Fig 6). Because of the contamination and comminution of the fracture, it was necessary to remove the bone fragments at the time of initial operation. Since the defect measured only one and one half inches in diameter, it was considered unnecessary, at that time, to repair it. Recovery was uneventful but the patient expressed a constant fear of further injury to the "soft spot" and was worried by the depressed scar which resulted.

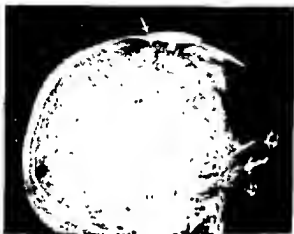


Fig 6—Small tantalum plate in place. note where arrow indicates the tip of one tab placed exactly in the diploë space.

For these reasons a tantalum plate was applied over the defect Dec 13, 1945. This plate was formed at the operating table. Recovery from this procedure was without incident. The patient has had no complaints and it is impossible to palpate the plate edges beneath the scalp.

#### SUMMARY AND CONCLUSIONS

Tantalum is a satisfactory metal for use in skull plating.

Fixation of cranioplastic plates to the skull is necessary.

Most skull defects should be closed.

A simple, satisfactory, one-piece method for fixed metallic skull plates has been described.

Two cases are presented to illustrate this tab-in-slot fixation procedure.

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## THE LATE DEFINITIVE TREATMENT OF GUNSHOT WOUNDS OF THE HEAD

ALFRED L. CONWAY, M. D., HERBERT CONWAY, AND CARTER ROBERT T. HENRICKS,  
NEW YORK, N. Y., MEDICAL CORPS, ARMY OF THE UNITED STATES

THE purpose of this communication is to present our experience with thirty cases of late injury to the head. These were cases in which there had been a primary decomposition of the wound of the skull and brain or in which the early surgical treatment had been inadequate. They were included in a group of 4,946 casualties from the campaign for the Philippine Islands.\* These patients were admitted to an Army general hospital in Hollandia, New Guinea, at a period varying from eight to twenty-nine days after injury. The problem was the surgical management of the late complications of war wounds of the head. The twenty cases which are the basis for this report, therefore, represent a selected group in that the patients had survived the original injury as well as the rigors of water transportation for a distance of 700 to 1,700 miles. In twenty-seven of the thirty cases the complications were due to infection. In twenty-five of these the infection was localized, meningitis developed in only two cases. All of these patients had been treated prophylactically with sulfonamide drugs or penicillin. Included in this report are examples of epidural abscess, cortical abscess, subcortical abscess, cerebral laceration, cerebral necrosis, depressed fracture of the skull, osteomyelitis of the skull, and combinations of these conditions. The striking similarity of the findings at the operating table in these cases served to clarify for our surgical staff the pathologic changes consequent to infection following war injuries of the head and to standardize the operative intervention because of the development of late complications. Thus this paper deals with the late treatment of gunshot wounds of the head. The indications for operation were the signs of intracranial infection, of persistent or progressive paralysis or of increased intracranial pressure. The fact that the series of 4,946 casualties included only sixty-two cases of skull fracture is not considered to be of statistical significance as to the frequency of cranial wounds in battle. However it may be mentioned that the missile caused injury to the brain in forty-seven of the sixty-two cases and that late surgical complications requiring operative surgery developed in thirty of these.

*General Condition of the Patients.*—Twenty of the thirty patients were in fairly good general condition at the time of arrival at this general hospital. Of the other ten, one was unconscious, three were semiconscious, two showed signs of meningitis, and four were acutely ill and febrile. Significant neurologic findings included hemiplegia, paraplegia, aphasia, ataxia, cranial nerve palsy.

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\*Conway, Herbert, and Collinwater, Kenneth D. Battle Casualties from the Philippine Islands, *Surgery* 20: 152, 1945.

amaurosis, and choked discs. Observation of the general condition of these patients and the state of their wounds at the time of admission to this hospital leads to a review of the therapy which was applied in the forward areas. All had received prophylactic sulfonamide therapy and in six cases penicillin had been given intramuscularly en route to this hospital. Supportive measures by means of parenteral fluids and transfusions of blood or plasma had been applied effectively from the time that the patients were seen at the battalion aid station until their admission to this hospital. Adequate neurosurgical débridement had not been done in any of these cases. Débridement and closure of the wound of the scalp had been done in only fourteen of the thirty cases. Eight of these sutured wounds became infected, six healed although there was underlying intracranial abscess. In the sixteen cases in which there had been no early operative surgical treatment, the wounds were grossly infected at the time of arrival at the hospital. In all probability the conditions of battle in which these soldiers were engaged afforded neither the necessary time nor the surgical equipment needed for neurosurgical débridement.

The medical records of many of these cases had been lost and in others the records were incomplete. Therefore, on arrival at this hospital, emphasis was placed on neurologic examination and on supportive treatment. Scalps were shaved, wounds were inspected and dressed; roentgenograms were taken to ascertain the exact location of the injury and to localize the depressed fragments of bone and the foreign bodies. All were treated with penicillin and sulfadiazine. Fluids were forced and transfusions of blood or plasma were administered as indicated. Penicillin was injected intrathecally at the time of diagnostic lumbar puncture. Careful eye, ear, nose, and throat examinations were made. In the care of paralytics, precautions were taken against the development of decubitus. Contractures were prevented by the use of splints and by physical therapy.

*Operative Procedure and Findings at Operation*—The procedure in operative surgery in these thirty cases included débridement of the wound with extension of incision of the scalp in such manner as to allow for adequate exposure and for closure of the scalp without tension. Because of the nature of the skull fractures in these cases and the presence of infection, débridement of the skull was done somewhat differently than is usual in the care of fresh injuries. Through a burr hole placed about 2 cm. from the peripheral extensions of the fracture, a rongeur was inserted to remove a circular section of bone surrounding the fracture of the skull (Fig. 1). Often there was low-grade osteomyelitis of the skull. This technique afforded excellent exposure for determination of the extent of intracranial injury and infection. In some cases fragments of fractured skull were depressed but the dura mater was not penetrated. In others the dura was perforated and fragments of bone were deep in the subcortical area of the brain. The degree of injury to the skull varied from small perforations of 1 cm. in diameter, to large, stellate, comminuted, depressed fractures. Removal of the calvarium was limited to the extent of the fracture of the inner table of the skull. As in depressed skull fractures caused by injury

in civilian life, the fractures of the inner table of the skull commonly were more extensive than those of the outer table. Because of infection of the skull it was necessary in several cases to remove the bone well beyond the area of fracture. In cases in which the dura had not been perforated, an abscess of the epidural space usually was found. At operation abscesses were isolated by packing thin strips of iodoform gauze into the epidural space about the margins of the bony

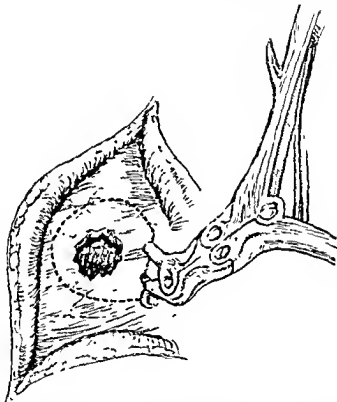


Fig. 1.—Illustrating the technique of debridement of infected skull fracture due to gunshot wounds. The central bony defect represents the point of entrance of the missile. The tables of the skull adjacent to the defect commonly are the site of low-grade chronic osteomyelitis. A burr hole at a distant site as shown allows for the removal of the infected section of bone in one piece without disturbing the granulation papilla which projects through it as shown in Fig. 2.

defect. In such cases the dura was not opened. The wounds were closed loosely around a soft rubber tube which was placed as a drain. In cases in which the dura had been penetrated, a fairly constant pattern was found. Through the dural defect there was a papilla-like projection (Fig. 2). This was composed of detached fragments of bone, necrotic cerebral tissue, clotted blood, hair, foreign material and granulation tissue. In most cases the dura and the pia-arachnoid were adherent to the cerebral cortex adjacent to the perforation of the meninges. After the dura was incised circumferentially around the defect, the torn and infected meninges were dissected carefully off the cortex exposing the

site of the injury to the brain. The subdural space was then sealed off by iodoform gauze packs or by electrocoagulation. The papilla and the center of the injured area were then excised using the electrosurgical knife. Pus, undriven fragments of bone, necrotic cerebral tissue, blood clots, and foreign material were removed by gentle suction and irrigation. The abscess cavity in the tract of the missile always contained the undriven fragments of bone. Commonly the missile was at a distant site in the brain or had made its exit from the skull. Let us visualize the effect of the missile. Its first impact perforates the skull carrying many small fragments of bone before it. The resistance offered by the cerebral tissue causes these fragments to lodge in the subcortical tissue while the missile continues onward. At operation the cavity was unroofed and effort was made to remove all of the fragments of bone without breaking through the wall of the abscess. Metallic foreign bodies were not removed unless readily accessible. The scalp was closed loosely about a soft rubber tube which extended into the abscess.

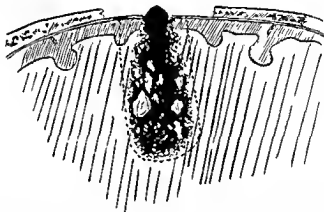


Fig. 2.—Sketch showing the papillary projection through the torn dura following removal of the section of perforated skull as shown in Fig. 1. In cases of cortical and subcortical abscesses due to gunshot this papilla was a constant finding. It was composed of depressed and detached fragments of bone, necrotic cerebral tissue, clotted blood, hair, foreign material, and granulation tissue. The comminuted fragments of skull are driven into the subcortical area. Apparently they are driven varying depths by the force of the missile. As the missile proceeds to a distant site in the brain or makes its exit from the skull, these bony comminutions form a pattern suggestive of the tail of a comet. The abscess is found around these depressed fragments of bone, not around the missile.

Intracranial abscess (epidural, cortical, or subcortical) was found in twenty-five cases. Report of the bacteriology of these abscesses is given in Table I. In four cases local cerebral necrosis was found. In one case there was a compound depressed fracture of the skull without associated intracranial infection. In all cases it held true that lesions manifested by paralysis were in the region of the motor strip or pyramidal tracts. In those cases in which the lesion was manifested only by the signs of increased intracranial pressure, abscesses were in the silent areas of the brain. In two cases in which a visual defect was the only indication for operation, the lesions were found in the occipital lobe.

*Postoperative Care.*—Therapy with sulfadiazine and penicillin was continued after operation. In addition, the abscess cavities were irrigated every

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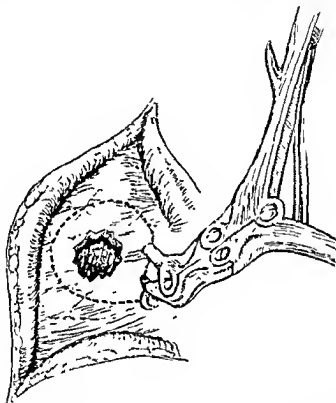


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TABLE II. (CONT'D)

CASE NO	MAJOR INDICATION FOR OPERATION	FINDINGS AT OPERATION	RESULT
20	No constitutional or localizing signs, infected wound	Depressed fracture of postparietal region with laceration of dura and brain; undriven bone fragments, brain necrosis, left	Complete recovery
21	No constitutional or localizing signs, infected wound	Depressed fracture of frontal bone with osteomyelitis and epidural abscess, right	Complete recovery
22	No constitutional or localizing signs, infected wound	Depressed fracture, epidural abscess, parietal region, left	Complete recovery
23	No constitutional or localizing signs, infected wound	Depressed fracture, epidural abscess, postparietal region, right	Complete recovery
24	No constitutional or localizing signs, infected wound	Depressed fracture, epidural abscess, parietal region, right	Complete recovery
25	No constitutional or localizing signs, infected wound	Huge depressed fracture of occipital, temporoparietal and frontal bones, epidural abscess, right	Complete recovery
26	No constitutional or localizing signs, infected wound	Depressed fracture, epidural abscess, frontal region, right	Complete recovery
27	Defect of visual red (homonymous)	Necrosis of brain, occipital region, left	No change
28	Partial blindness; convulsive seizures	Small subcortical abscess and epidural abscess, occipital region in midline	Seizures relieved, no improvement in vision
29	Signs of meningitis, paralysis of both lower extremities, semi-conscious, aphasic	Depressed fracture, huge subcortical abscess ruptured into lateral ventricle, suppurative meningitis, frontoparietal region, left	Died
30	Generalized convulsive seizures, no localizing signs	Through and through wound of both frontal regions, huge abscess, left frontal lobe ruptured into lateral ventricle, suppurative meningitis	Died

two hours through the drainage tube using solution of penicillin (250 units to 1 c.c.). Increased intracranial pressure was relieved by repeated spinal punctures. Fluids were not restricted. Drains were left in place for five days after operation unless there were signs of cortical irritation. In three cases the occurrence of jacksonian epilepsy necessitated the removal of the drain. A detail of great importance is the early institution of physiotherapy to the paralyzed extremities. In some cases electrical stimulation of the affected muscles was used. Patients were encouraged to get out of bed as soon as their general condition and their strength permitted. Occupational therapy and recreational therapy were employed while these soldiers awaited transportation to the United States.

*Results Following Operation.*—Of particular interest are the clinical results following operative surgery. Five of the nine patients with hemiplegia (Cases 1 to 9) recovered completely from paralysis and two were greatly improved. Only two were unimproved. The two patients in whom there was paralysis of the lower extremities (Cases 10 and 11) recovered sufficiently to walk out of the hospital unassisted by braces. In seven out of eight cases in which operation was performed because of signs of increased intracranial pressure (Cases 12 to 19)



TABLE I. BACTERIOLOGY OF CEREBRAL ABSCESS SECONDARY TO GUNSHOT WOUNDS OF THE HEAD

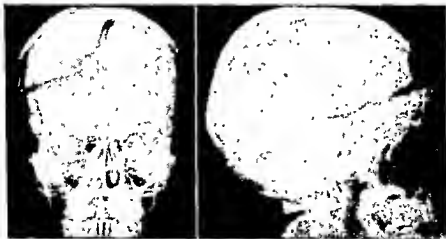
ORGANISM	NUMBER OF CASES
Organisms of the proteus group	4
Hemolytic staphylococcus aureus	4
Beta hemolytic streptococcus	2
Nonhemolytic staphylococcus	1
Nonhemolytic streptococcus	1
Anaerobic streptococcus	1
Anaerobic gram positive rods	1
Gram positive micrococci	1
Organism not identified	15
Total	50

TABLE II. LATE COMPLICATIONS OF WAR WOUNDS OF THE HEAD  
(ANALYSIS OF 30 CASES)

CASE NO.	MAJOR INDICATION FOR OPERATION	FINDINGS AT OPERATION	RESULT
1	Hemiplegia, complete	Subcortical abscess with clot, frontoparietal region, left	Ambulatory but with weakness of affected extremities
2	Hemiplegia complete	Small subcortical abscess, frontal parietal region, left	Complete recovery
3	Hemiplegia complete	Small subcortical abscess, frontal parietal region, left	Complete recovery
4	Hemiplegia, incomplete	Depressed fracture, epidural abscess, parietal region, left	Complete recovery
5	Hemiplegia, complete, at first, semiconscious	Large subcortical abscess, frontal parietal region, left	Ambulatory, sphincter improved
6	Hemiplegia, incomplete	Subcortical abscess, temporo-parietal region, left	Ambulatory but with paralysis of lower extremity
7	Hemiplegia, incomplete	Large subcortical abscess with much brain edema, frontoparietal region, left	Return of function of upper extremity; no improvement of lower extremity
8	Hemiplegia complete	Large subcortical abscess with cerebral edema, frontoparietal region, right	No improvement
9	Hemiplegia, incomplete	Small subcortical abscess, frontoparietal region, left	No improvement
10	Paralysis of both feet	Depressed fracture of the vertex and epidural abscess over the longitudinal sinus	Ambulatory with residual weakness of muscles of left foot
11	Paralysis of both feet	Depressed fracture and epidural abscess over the vertex to the right of longitudinal sinus	Ambulatory with residual weakness of left foot and ankle
12	Blurred disc margins	Small subcortical abscess, frontal lobe, left	Complete recovery
13	Blurred disc margins	Large subcortical abscess, frontal lobe, right	Complete recovery
14	Blurred discs	Small area of necrosis of cerebral cortex, frontal lobe, right	Complete recovery
15	Clotted discs	Large subcortical abscess, frontal lobe, right	Complete recovery
16	Bilateral choked discs, seventh nerve paralysis	Large subcortical abscess, frontal lobe, right	Complete recovery
17	Bilateral sixth nerve paralysis, drowsiness	Large subcortical abscess, frontal lobe, left	Recovery, nerve paralysis improved
18	Drowsiness, bilateral choked discs, respiratory depression	Subcortical abscess, parieto-occipital region, right	Complete recovery
19	Unconscious; infected wound	Depressed fracture, epidural abscess, temporo-parietal region, left	Regained consciousness; residual mental retardation



Fig. 3 (Case 5)—In this photograph the hemostat points to the scar which represents the healed point of entry of the bullet. Progressing anteromedially the bullet made its exit from the site of fungous cerebri in the left frontal region. The patient had complete right hemiplegia which was accounted for by the finding of a large abscess directly under the motor strip and in the path of the bullet. He recovered from hemiplegia.



A

B

Fig. 4 (Case 5)—Anteroposterior and lateral views of skull showing the extensive and elevated fracture. This had been caused by an enemy machine-gun bullet which entered the left parieto-occipital area and made its exit from the skull in the left frontal region.

there was complete recovery. The eighth patient (Case 19) recovered physically but mental retardation persisted. Complete recovery followed in seven cases in which surgery was carried out because of infected wounds overlying a depressed fracture (Cases 20 to 26). Two patients in whom the injury was to the occipital lobe (Cases 27 and 28) failed to show improvement. In two patients in whom cerebral abscess had perforated into the lateral ventricle of the brain the patients succumbed despite drainage of the abscess (Cases 29 and 30).

A summary of results following operation for the late sequelae of gunshot wound of the head shows that of these thirty cases, sixteen patients recovered completely, five showed dramatic improvement, three improved, four failed to improve, and two died. In Table II are listed for each individual case the indications for operation, the findings at the operating table, and the results at the time the patients embarked for the United States.

In this brief presentation no attempt is made to discuss each case in detail. Since these cases fall roughly into six groups, exemplary case reports are presented. Cases are numbered according to their sequence in Table II. Cases 1 to 9 are those in which hemiplegia was found in association with abscess of the parietal area of the brain. The following case report is typical of those in this group, with hemiplegia and aphasia due to subcortical abscess of parietal lobe, fungous external surgical drainage forty-eight days after injury, wound healing by skin graft, and recovery from paralysis and aphasia.

**CASE 5.** This is the case of a 23-year old, white sergeant in the infantry who was wounded in action Nov. 11, 1944, at Leyte, Philippine Islands. An enemy machine gun bullet entered the left parietal region of the skull and made its exit through the frontal area. No operative treatment had been given in the forward area. Records indicated that sulfadiazine and penicillin had been given for ten days prior to arrival at this general hospital on Dec. 13, 1944. Examination revealed a semiconscious white man. Temperature was 101° F.; pulse, 116, respirations, 25, blood pressure, 130/80, red blood cells, 3,000,000; white blood cells, 12,000, hemoglobin, 45 per cent. The patient responded to simple commands. The small scar of the healed wound of entry was over the left parieto-occipital region. A beta hemolytic staphylococcus was recovered on culture of thick yellow pus which drained from the wound. The photograph (Fig. 3) demonstrates that the machine gun bullet entered the left parieto-occipital region, traversed the left cerebral hemisphere, and made its exit from the skull in the left frontal region. Through this wound necrotic, pulsating, cerebral tissue protruded. Roentgenograms (Fig. 4) demonstrated the extensive bursting type of fracture of the left occipital, parietal and frontal bones. The heart and lungs were normal. There was some abdominal distention. Neurologic examination revealed cervical rigidity. The patient was completely aphasic. There was paralysis of the right facial nerve (central type). Vision could not be tested satisfactorily. Right hemiplegia was manifested by flaccid paralysis of the right upper extremity and spastically with weakness of the right lower extremity. He flexes were hyperactive on both sides. Sustained ankle clonus and Babinski reflexes were elicited bilaterally. Spinal tap done at the time of admission revealed normal spinal fluid not under increased pressure. The patient was treated with intravenous fluids, transfusions of blood, and penicillin intramuscularly and intrathecally. There was gradual improvement in the general condition though he remained in a semiconscious state. An abscess of the scalp developed in the left frontal region. This was incised and drained. A few days later the patient had a generalized convulsive seizure followed by copious drainage of pus from the wound of the left frontal region. The patient's general condition again improved. At operation on January 5 (forty-eight days after injury) the wound of exit was excised and several large fragments of bone were removed. The necrotic cerebral tissue was removed from the frontal

tive of the group, with depressed skull fracture without localizing signs but with large infected wound and extradural abscess, follows:

**CASE 25**—This 21 year old infantryman was wounded in action by an enemy shell fragment Feb. 10, 1945, at Luzon, Philippine Islands. There was no primary operative treatment. The patient was transported to Hollandia, New Guinea, via hospital ship, arriving at this general hospital Feb. 25, 1945. The patient was ambulatory and felt quite well. Temperature, pulse, and respirations were normal. Physical examination revealed nothing of importance save the wound of the head. There was an infected, granulating wound of the right parieto-occipital region. The wound measured 6 by 3 cm. Its surface was covered with a dry crust under which there was necrotic soft tissue. A depressed fracture was found on exploration with a blunt instrument. Apparently this void wound represented the confluent points of entry and exit of a missile which had struck the skull tangentially. X-ray examination revealed an extensively comminuted, depressed fracture involving the frontal, parietal, and temporal bones. At operation on Feb. 27 (seventeen days after injury) it was revealed that despite the extent of this depressed fracture, the dura had not been lacerated. There was a large extradural collection of pus and granulation tissue. All depressed fragments of bone were removed. The wound was sutured loosely over a soft rubber tube through which irrigation with a solution of penicillin was carried out. The tube was removed on the fifth day after operation. The patient made an uneventful convalescence and embarked for the United States on March 8, 1945.

Observation of the thirty patients included in this report has established the impression that cerebral infection following war wounds of the head tends to localize, often forming an abscess about the indriven fragments of bone. Experience with this small group of cases does not warrant conclusions as to whether or not therapy with sulfonamide drugs and penicillin favors this localization. Cases 29 and 30 bring attention to the fact that although cerebral abscesses due to missile wounds tend to localize, it does not follow that these abscesses will remain limited in size. These two cases are discussed together because both are examples of fatality due to rupture of cerebral abscess into the lateral ventricle. The relatively slow development of abscess following war wounds of the head may allow for firm healing of wounds of scalp and skull before the pressure within the abscess reaches its highest point. Consequently, rupture into the lateral ventricle may be expected in neglected cases. The following case report is given as an example, with meningitis due to rupture of a subcortical cerebral abscess into the lateral ventricle; death.

**CASE 29**—This 25 year old private of the engineering corps was wounded by a shell fragment on Feb. 6, 1945, in Luzon, Philippine Islands. Debridement of the skull and scalp with primary suture was done at an evacuation hospital eight hours after injury. The patient was admitted to this hospital in critical condition on March 28. He was semiconscious and febrile. There was marked cervical rigidity. Temperature was 100° F; pulse, 88; respirations, 18; blood pressure, 120/85; red blood cells, 3,000,000; white blood cells, 16,000; hemoglobin, 62 per cent. Through a defect of the skull and scalp in the left parieto-frontal region, necrotic brain fungus presented. There was paralysis of the seventh nerve on the right side (central type) and there was divergent squint. There was flaccid paralysis of both lower extremities and urine was overflowing from the distended bladder. Spinal fluid was cloudy and the pressure was 180 mm. Roentgenograms showed a defect of the skull in the left parietal region. Treatment at first was by means of supportive measures. Penicillin was given intrathecally. The clinical records were inadequate but it was apparent from the surgeon's note that debridement of the scalp and skull had been carried out but that the meninges and brain had not been disturbed at the primary operation. When, therefore, five

... of bone was exposed on the opposite side where a metallic fragment ... the wound of entrance over the ... a circular area of skull surrounding the per ... The wound papilla like process is composed of granulation tissue, ... and but projected from the torn dura mater to plug ... The dura mater about the papilla was excised. The ... the electroencephal unit. Thirty cubic centi ... from an abscess deep in the subcortical area of ... was recovered on culture of this pus ... fragments of bone were removed from the wall of the ... of the crura in which cerebral abscess develops ... the muscle perforated the skull carrying before it a ... the path of the metallic fragment at a depth of 2 ... The muscle progressed onward coming to rest in the ep ... from the skull depending upon the force of ... the abscess cavity was unroofed and the wound was ... about a soft rubber tube



Fig. 1. Views of skull showing intruded fragments of bone about which a subcortical abscess was centered

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by tangential impact from the missile. Neurologic examination revealed that there was no disturbance of function of the cranial nerves. Sensory examination was normal except for hypesthesia over the right foot and hypesthesia of the left foot extending up to the middle third of the left leg. There was paralysis of both feet. Babinski reflexes were present on both sides. The patellar and Achilles reflexes were hyperactive on both sides. There was sustained ankle clonus on the right. Neurologic examination was otherwise normal. Roentgenograms showed a depressed, comminuted fracture directly over the median sagittal suture of the skull. There were no retained foreign bodies. Photograph of lateral x ray view of the skull is shown in Fig 5. Transfusions of blood were given and therapy with penicillin was continued. At operation on Oct. 30, 1944, ten days after injury, the infected wound was excised and the depressed fractures of the two parietal bones, near the medial sagittal line of the skull were exposed. Depressed fragments of bone were removed. There was an epidural abscess overlying the longitudinal sinus. The dura mater had not been penetrated. The epidural space was protected from the abscess by thin strips of iodoform gauze packing and the wound of the scalp was closed about a soft rubber tube. Hemolytic *Staphylococcus aureus* was recovered on culture of the purulent exudate. Postoperatively the wound was irrigated, every two hours with penicillin solution (250 units per cubic centimeter). The iodoform gauze packs were removed on the fourth postoperative day and the tube was removed on the fifth day. The wound healed by second intention. The paralysis of the feet gradually diminished and the patient was able to walk on December 5. Muscle training was instituted and the patient embarked for the United States on December 16. At that time he walked unassisted. There was residual weakness of the tibialis anterior group of muscles on the left and paresis of the plantar flexors on the right.

In eight patients (Cases 12 to 19) the clinical pictures were similar in that the significant physical signs referable to increased intracranial pressure were the findings on ophthalmologic examination. In these cases the areas of cerebral necrosis or abscess were located either in the frontal or in the occipital lobes. In three of these patients there were signs (other than choked discs) of increased intracranial pressure. Clinicians were impressed with the fact that in several cases in which large abscesses were encountered, the presence of blurring of the optic fundi was the sole clinical sign which indicated that an intracranial lesion existed. Of the eight patients in this group, seven recovered completely following operation. The case history of one of these patients follows, showing drowsiness, respiratory depression and choked discs due to subcortical abscess in the parieto-occipital region, surgical drainage fifteen days after injury, and complete recovery.

CASE 18.—This 19 year old white infantryman was wounded by fragments of a hand grenade on Dec. 10, 1943, at Leyte, Philippine Islands. He was transported to Hollandia, New Guinea, by hospital ship arriving December 21. There had been no operative surgical treatment. Penicillin had been given for eight days prior to admission to this general hospital. He was ambulatory but complained of left parietal headache. Temperature was 99.4° F., pulse, 60; respirations, 20, blood pressure, 110/85; red blood cells, 3,500,000; white blood cells, 12,500, hemoglobin, 80 per cent. There was an infected wound with draining sinus over the right parietal region of the scalp. X ray examination revealed a perforated fracture of the skull in the right occipital area, a cluster of small comminuted fragments of bone in the occipital region of the right cerebral hemisphere, and a metallic foreign body (1 cm. in diameter) in the substance of the brain in the left parieto-occipital area. Within sixteen hours after admission, this patient became increasingly drowsy. The pulse rate dropped to 51 and the respirations to 12 per minute. Spinal fluid pressure was 220 mm. Dynamics were normal and the fluid was clear. Neurologic examination was negative save for the findings on ophthalmologic examination. Both optic discs were choked. Based on experience with earlier cases the abscess was presumed to be in the right occipital lobe centered

lobe using the electrosurgical unit. The tract of the missile was probed and a large subcortical abscess was encountered directly under the motor strip. The cavity was irrigated with penicillin and the wound of the scalp was closed loosely about a soft rubber tube which extended into the abscess. After operation the patient regained consciousness and the general condition improved rapidly. For the first few days after operation the abscess was irrigated every two hours with penicillin solution (250 units per cubic centimeter). The hemiplegia diminished and on the twenty-fifth day after operation the patient was able to walk with assistance. A thick split graft was applied to the wound of the forehead on February 25. The patient regained motor control of the extremities. The facial paralysis diminished. Speech returned slowly. In the postoperative care of this patient intensive physical therapy was given to affected muscles and speech training was emphasized. At the time of evacuation to the United States on March 9, 1945, he could talk in simple phrases and walked about without assistance.

There were two patients (Cases 10 and 11) in whom there was paralysis of the lower extremities due to depressed fracture in the region of the vertex of the skull, with epidural abscesses overlying the longitudinal sinus and the upper portion of the motor strips on both sides. Both of these patients recovered from paralysis following elevation of the fracture and simple drainage of the abscesses. An exemplary case record follows, in which there were paralysis of both feet due to depressed fracture over the vertex of the skull with epidural abscess, surgical drainage ten days after injury, complete healing of the wound, and recovery from paralysis.



Fig. 5 (Case 10).—Lateral x-ray view of skull showing fracture caused by tangential impact of an artillery shell fragment. In this case an epidural abscess had formed over the longitudinal sinus. The wounds of entry and exit were confluent over the vertex of the skull.

CASE 10.—This 19-year-old paratrooper was wounded in action by an artillery shell fragment on Oct. 20, 1944, at Leyte, Philippine Islands. No operative treatment was given in the forward area. The patient was evacuated by LST and arrived at this hospital on October 23. Penicillin had been given intramuscularly while en route. Examination revealed a well-developed, malnourished, pale, white man who was conscious and mentally alert. Temperature was 99° F.; pulse, 85, respirations, 18, blood pressure, 120/80, red blood cells, 3,000,000, white blood cells, 10,000, and hemoglobin, 60 per cent. The heart, lungs, and abdomen were normal. Examination of the head revealed a dirty, infected wound over the vertex of the skull through which a depressed fracture of the skull could be seen. The furrowed wounds of entry and exit were confluent. Apparently the fracture of the skull had been caused

tive of the group, with depressed skull fracture without localizing signs but with large infected wound and extradural abscess, follows:

**CASE 25**—This 21 year old infantryman was wounded in action by an enemy shell fragment Feb 10, 1945, at Luzon, Philippine Islands. There was no primary operative treatment. The patient was transported to Hollandia, New Guinea, via hospital ship, arriving at this general hospital Feb 25, 1945. The patient was ambulatory and felt quite well. Temperature, pulse, and respirations were normal. Physical examination revealed nothing of importance save the wound of the head. There was an infected, granulating wound of the right parietooccipital region. The wound measured 6 by 3 cm. Its surface was covered with a dry crust under which there was necrotic soft tissue. A depressed fracture was found on exploration with a blunt instrument. Apparently this oval wound represented the confluent points of entry and exit of a missile which had struck the skull tangentially. X-ray examination revealed an extensively comminuted, depressed fracture involving the frontal, parietal, and temporal bones. At operation on Feb 27 (seventeen days after injury) it was revealed that despite the extent of this depressed fracture, the dura had not been lacerated. There was a large extradural collection of pus and granulation tissue. All depressed fragments of bone were removed. The wound was sutured loosely over a soft rubber tube through which irrigation with a solution of penicillin was carried out. The tube was removed on the fifth day after operation. The patient made an uneventful convalescence and embarked for the United States on March 8, 1945.

Observation of the thirty patients included in this report has established the impression that cerebral infection following war wounds of the head tends to localize, often forming an abscess about the indurated fragments of bone. Experience with this small group of cases does not warrant conclusions as to whether or not therapy with sulfonamide drugs and penicillin favors this localization. Cases 29 and 30 bring attention to the fact that although cerebral abscesses due to missile wounds tend to localize, it does not follow that these abscesses will remain limited in size. These two cases are discussed together because both are examples of fatality due to rupture of cerebral abscess into the lateral ventricle. The relatively slow development of abscess following war wounds of the head may allow for firm healing of wounds of scalp and skull before the pressure within the abscess reaches its highest point. Consequently, rupture into the lateral ventricle may be expected in neglected cases. The following case report is given as an example, with meningitis due to rupture of a subcortical cerebral abscess into the lateral ventricle; death.

**CASE 29**—This 25 year old private of the engineering corps was wounded by a shell fragment on Feb 6, 1945, in Luzon, Philippine Islands. Débridement of the skull and scalp with primary suture was done at an evacuation hospital eight hours after injury. The patient was admitted to this hospital in critical condition on March 23. He was semiconscious and feeble. There was marked cervical rigidity. Temperature was 100° F; pulse, 88; respirations, 18; blood pressure, 120/85; red blood cells, 3,000,000; white blood cells, 16,000; hemoglobin, 62 per cent. Through a defect of the skull and scalp in the left parieto-frontal region, necrotic brain fungus presented. There was paralysis of the seventh nerve on the right side (central type) and there was divergent squint. There was flaccid paralysis of both lower extremities and urine was overflowing from the distended bladder. Spinal fluid was cloudy and the pressure was 180 mm. Roentgenograms showed a defect of the skull in the left parietal region. Treatment at first was by means of supportive measures. Penicillin was given intrathecally. The clinical records were inadequate but it was apparent from the surgeon's note that débridement of the scalp and skull had been carried out but that the meninges and brain had not been disturbed at the primary operation. When, therefore, five



about the indriven chips of bone rather than on the opposite side where a metallic fragment had lodged. On December 25 (fifteen days after injury) the wound of entrance over the right parieto occipital area was excised and a circular section of skull surrounding the perforation was removed. The typical papilla like projection, composed of granulation tissue, clotted blood, debris, necrotic brain and hair, projected from the torn dura mater to plug the perforation in it and in the skull. The dura mater about the papilla was excised. The epidural and subdural spaces were sealed with the electrosurgical unit. Thirty cubic centimeters of thick, yellow pus were evacuated from an abscess deep in the subcortical area of the right occipital lobe. Hemolytic staphylococcus was recovered on culture of this pus. Along with the pus, numerous small fragments of bone were removed from the wall of the abscess. The operative findings were typical of the cases in which cerebral abscess develops after injury by a missile. Apparently the missile perforated the skull carrying before it a cluster of bony particles which lodged in the path of the metallic fragment at a depth of 2 to 3 cm below the cerebral cortex. The missile progressed onward, coming to rest in the opposite cerebral hemisphere or making its exit from the skull, depending upon the force of its unspent momentum. In this case the abscess cavity was unroofed and the wound was irrigated with penicillin solution. The scalp was sutured loosely about a soft rubber tube



Fig 6—Front and side views of skull showing indriven fragments of bone about which a subcortical abscess was centered

As soon as the pus had been evacuated the patient became talkative and stated that the head ache had been relieved. Postoperative therapy was carried out (as in Cases 5 and 10 reported previously). The patient made an uneventful recovery. The optic fundi were normal and vision was unimpaired at the time of embarkation to the United States on the thirtieth day after injury.

Cases 20 to 26 comprised a group of cases in which, in the absence of neurologic or localizing signs, surgical exploration was necessary because of infected wounds overlying depressed skull fractures. Findings at operation in these seven cases were as follows: epidural abscess, five cases, epidural abscess with osteomyelitis of the skull, one case, cerebral necrosis about indriven fragments of bone, one case. All of these patients made an uneventful recovery following excision of the chronically infected wounds, elevation of the depressed fractures, and irrigation of the wound with penicillin. A case report representa-

## AFFERENT CONDUCTION VIA THE SYMPATHETIC GANGLIA INNERVATING THE EXTREMITIES

FRANCIS D. THREADGILL, M.D., WASHINGTON, D. C.

(From the Department of Anatomy, Georgetown University School of Medicine)

WHILE there is a general denial that afferent sensations are transported via the sympathetic innervation of the extremities, experiments conducted for the purpose of establishing the existence of such pathways continue to be of great interest. A physiologic demonstration of afferency within the gray rami communicantes and the sympathetic ganglia innervating the extremities will eliminate much of the confusion which exists in our knowledge of pain conduction.

This paper deals with afferent conduction in the spinal nerve below the gray rami communicantes to the cord in the region of the lumbosacral plexus.

### REVIEW

Ransom and Billingsley<sup>1</sup> have described both myelinated and unmyelinated fibers in the gray rami communicantes of the cat. Kuntz and Farnsworth,<sup>2</sup> studying the sympathetic trunks and gray rami communicantes in the cat, stated that certain fibers in these structures supplying the extremities must be regarded as afferent from an anatomic standpoint.

Moore and Singleton<sup>3</sup> showed that the arterial injection of lactic acid is intensely painful to animals after a sympathectomy, and the majority of workers feel that sympathetic ganglionectomy does not interfere with afferent sensations. Since Moore and Singleton also were able to show that there is no painful response following section of the peripheral nerve to the part, the conclusion was drawn that the blood vessels receive their sensory supply from the peripheral nerves and not from the sympathetic nerves per se.

The present concept of vascular innervation of the extremities is based on the results of this work and is as follows: All the vessels and pilosebaceous apparatus of the extremities receive innervation from the peripheral nerves with efferent fibers only from the sympathetic ganglia. These fibers enter the peripheral spinal nerves by way of the gray rami communicantes. Consequently, the explanation of the relief of pain, in a human being, following sympathectomy is that vascular spasm is relieved by sympathetic interruption.

de Takats,<sup>4</sup> however, demonstrated that in many cases of causalgia there is no vasospasm, but rather there is vasodilatation. In the presence of vasodilatation, the benefit obtained by sympathectomy cannot be explained on the basis of the concept stated previously.

Livingston's<sup>5</sup> theory of internunciate neurons within the spinal cord is generally accepted as the explanation of the good results which follow sympathetic interruption, although actually the procedure remains on an empirical

days after admission to this hospital, the cervical rigidity was diminishing and the patient was slightly improved, surgical exploration was advised. It was reasoned that the signs of meningitis might have been due to extension of an abscess toward the pia arachnoid and that drainage of such an abscess offered the best hope for recovery. At operation on March 29 (thirty-one days after injury) a large subcortical abscess of the left frontoparietal area was drained. The abscess extended into the lateral ventricle. Copious amounts of thin purulent material were evacuated. Suppurative *epiduritis* and *meningitis* were in evidence. After operation the signs of meningitis persisted and the patient died on March 31. Post mortem revealed that the abscess cavity was 8 cm. in greatest diameter. It was oblong in shape and occupied a position extending into the subcortical areas of the frontal, parietal, and temporal areas of the cerebral hemisphere. It had eroded or compressed most of the tissue of the cerebral hemisphere and had ruptured into the anterior horn of the ventricle. There was cellular infiltration of the entire left cerebral hemisphere and generalized suppurative inflammation of the meninges.

#### SUMMARY AND COMMENT

An analysis is presented of thirty cases of missile injury to the head in which neurosurgical exploration was not carried out until eight to fifty-one days after injury. There were twenty-seven cases of intracranial abscess. Ten of these were extradural abscesses while seventeen were cortical or subcortical. In three cases of depressed fracture there was laceration of meninges and brain. Regional paralysis together with x-ray evidence of depressed fragments, has served to make localization of these abscesses relatively easy. Commonly the point of entry of the missile is marked by an infected wound. Invariably the abscess is centered about the dislocated fragments of bone, not around the missile. The metallic foreign body often is at a distant site in the cranial cavity or may have made its exit from the skull. Persistent or progressive paralysis, wound infection or findings on ophthalmologic examination have presented the indications for operation. Of these thirty patients who developed complications which were the sequelae of infection of war wounds of the head, twenty-eight survived operation. Following primary operation performed many days after injury, sixteen patients recovered completely, five showed dramatic improvement, three improved, four failed to show improvement, and two died. The mortality rate in this series of cases is 6.6 per cent.

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Livingston's<sup>5</sup> theory of internunciate neurons within the spinal cord is generally accepted as the explanation of the good results which follow sympathetic interruption, although actually the procedure remains on an empirical

basis. My experiments, I believe, tend to provide a more satisfactory explanation of the relief of pain afforded by sympathectomy, and, in addition, show that certain afferent impulses from the extremities are blocked by sympathetic ganglionectomy.

There are visceral reflexes in the abdominal viscera which certainly are completed without reaching the spinal cord,<sup>8</sup> but there is little evidence, up to the present, that similar reflexes of the extremities are completed outside the cord. Most anatomists find such a concept untenable because of the absence of actual and separate sympathetic nerves to the vessels and pilosebaceous apparatus of the extremities.

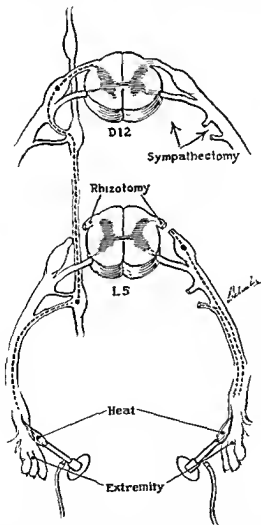


Fig. 1 (Preparation 1).—Showing bilateral posterior rhizotomy of nerve root to leg with unilateral sympathetic ganglionectomy. Painful sensations from heat are manifested by reaction on the nonsympathectomized side only. The anterior roots are undamaged.

Dogiel,<sup>7</sup> in 1896, showed that both motor and sensory nerve cells are present in the stellate ganglia of dogs, and he believed that visceral reflexes are completed in the sympathetic ganglia

Foerster and Gagel<sup>8</sup> maintained that pain impulses may travel by way of the sympathetic ganglionic chain and enter the cord through extrasegmental levels. Like Le Riche and Fontaine,<sup>9</sup> they believed that these impulses were carried to the ganglia via the perivascular plexii

Since all sensation from the extremities travels by way of the peripheral nerves<sup>10</sup> and since sympathetic ganglionectomy relieves pain in many cases, including those of vasodilatation, the assumption that at least part of the sensory impulses are relayed to the sympathetic ganglia on their way to the cord is justified

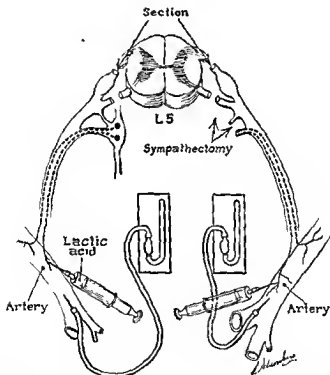


Fig 2 (Preparation 2) —Showing bilateral section of both anterior and posterior nerve root with unilateral sympathetic ganglionectomy. Lactic acid injection of artery of leg shows blood pressure changes on nonsympathectomized side only

#### EXPERIMENTAL OBSERVATIONS

In order to substantiate such an assumption, a preparation was made as is shown in Fig. 1. Following a preliminary removal of the sympathetic ganglia innervating one lower extremity, a bilateral posterior root section was performed to the extent that no further painful responses were elicited on the sympathetomized side. Since identical painful stimulation of the nonsympathectomized side produced a response manifested by kicking, one may believe

that at least a portion of painful sensation travels by way of the sympathetic ganglia and enters the cord through extrasegmental levels. The possibility that sensation had entered the cord via the anterior root was recognized and a second preparation, as is shown in Fig 2, was made in order to prove this had not happened

For this preparation unilateral sympathectomy was performed and bilateral section of both the anterior and the posterior root was done and was sufficiently extensive to eliminate response, on the sympathectomized side, to the stimulation produced by the injection of lactic acid into an artery. Since the anterior roots were sectioned, response was necessarily demonstrated by blood pressure variations rather than by kicking or other motion. The use of lactic acid as a means of stimulation on the nonsympathectomized side, however, produced immediately a sudden and marked fall in the blood pressure. This result demonstrated that vascular reflex response may be completed entirely outside the cord, because with both anterior and posterior roots severed, there was no possibility that afferent sensations had entered the cord by these routes.

*Methods.*—Through the courtesy of the Georgetown University Department of Pharmacology, experiments were conducted on dogs in the laboratory of pharmacology during the winter and spring of 1946

*Dog 1*—This dog was used as a preliminary experiment. Under nembutal and ether anesthesia a left sympathectomy, equal in extent to the succeeding ones, was performed using an anterior retroperitoneal approach. The incision was closed and the animal was allowed to recover. Ten days later this animal (a 4 month old dog) was operated upon, in the prone position under nembutal and ether anesthesia, and the spinal cord was severed at the first lumbar. The foot pads were then stimulated with flame and the left (sympathectomized) side was observed to react whereas the right side did not.

*Dog 2*—Under ether anesthesia the left sympathetic ganglionic chain was removed, through a lumbar extraperitoneal approach, from the first lumbar sympathetic ganglion to its conclusion. A laminectomy was then performed from the second lumbar vertebra through the anterior one half of the sacral plate. The dura was opened to expose the cord, and the posterior roots of the fourth lumbar to the third sacral were then sectioned bilaterally, at the point where all filaments were united. Immediately on completion of the operation, stimulation (flame of a Bunsen burner) was applied to the foot pads of the animal. The right leg reacted at once with a moderate kicking motion. The left leg did not react at all.

*Dog 3*—The experiment used on Dog 2 was repeated and the same result was obtained.

*Dog 4*—Under ether anesthesia a left lumbar sympathectomy was done and the cord was exposed in the same manner as in Dog 2. Both anterior and posterior nerve roots, beginning with the first sacral and proceeding caudad and cephalad, were sectioned until no further twitching of the legs occurred (section included nerve roots from the fourth lumbar through the third sacral). The left femoral artery was then exposed, just above the knee, and a cannula, pointing toward the heart, was placed in the artery. The artery was clamped distal to the cannula. As soon as a preliminary recording of the blood pressure was made on the kymograph, 10 c.c. of a 10 per cent solution of lactic acid were injected rapidly into the artery, below the recording cannula and clamp (so that the injection could not directly affect the pressure). The solution entered the artery in the direction of the normal blood flow. No change was noted in the blood pressure during a fifteen second observation period.

Next the right femoral artery was exposed cannulated in the same manner, and 10 c.c. of a 10 per cent solution of lactic acid were injected, below the cannula, into the artery.

Within one second the blood pressure dropped as shown in Fig. 3. The blood pressure then began to rise evenly and in fifteen seconds it had returned to the base level. The animal was then destroyed.

The reaction of Dog 1 supported the observations made by Wolf and Hardy<sup>11</sup> that following a sympathectomy an extremity, not otherwise damaged neurologically, reacts more sensitively to thermal changes. A reasonable explanation of this occurrence, which will be alluded to again, is that changes in the sympathetic afferents (which must be largely C fibers)<sup>12</sup> render the remaining central afferent fibers more sensitive to pain. It is interesting to conjecture that this increased sensitivity may account for the intractable pain of certain causalgic states, which have obviously diseased sympathetically innervated organs. Such phenomena are in contrast to the condition seen in Raynaud's disease in which sympathectomy produces relief of vessel spasm.

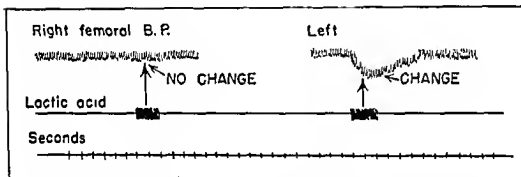


Fig. 3 (Preparation 2) — Showing blood pressure changes following lactic acid injection in the right or nonsympathectomized femoral artery. No change occurred on the left (sympathectomized) side.

#### COMMENT

Sympathetic afferents from the extremities are probably similar in function to the viscerosensory fibers in the splanchnic trunks. The location of the cell body, however, will be discussed in a future article.

These present experiments indicate that blocking of the sympathetic nerves can be placed on a sound anatomic and physiologic basis because, in addition to efferent fibers being interrupted, afferent fibers are interrupted.

The relief of pain afforded clinically by paravertebral ganglionic block and/or sympathectomy in certain morbid processes may be due to the relief of vasospasm or the blocking of afferent impulses from the vessels and piloschlaecous apparatus of the extremities, or both.

It is probable that afferent impulses from involuntary structures pass primarily to the sympathetic ganglia for integration with the sympathetic efferents, before entering the cord. In early morbid states, this same mechanism produces the pain which can be relieved by sympathectomy. However, with the progression of morbidity, the central spinal nerves appear to be affected, and this central nerve involvement accounts for the poor results obtained from sympathetic interruption in cases of fixed causalgic lesions.<sup>13</sup>





## SURGICAL MANAGEMENT OF VASCULAR LEG ULCERS

HOWARD C. REFS, M.D., AND JOHN G. SLEVIN, M.D., DETROIT, MICH.

(From the Peripheral Vascular Clinic, The Grace Hospital)

ULCERS of the lower extremity are primarily surgical cases. Too often surgery is thought of only after the patient has been given long periods of local treatment. Too much is expected of local treatment, one form of medication after another being tried before surgery is suggested.

After more than ten years' experience with such cases in the Peripheral Vascular Clinic of The Grace Hospital, we are convinced that the surgical approach to peripheral vascular ulcers not only shortens the period of treatment but also, in many cases, offers the only chance for a lasting cure.

A proper appreciation of the etiology of leg ulcers demonstrates why this assertion is correct. Although such ulcers may be divided into ischemic, due to occlusive arterial disease, and varicose, when venous congestion is the cause, yet the local effects are quite similar. In both types of ulcer there are local malnutrition and lowered tissue resistance. When an ulcer forms in tissue with impaired blood supply, the natural healing powers are diminished, and the ulcer tends to persist. If it does heal it is prone to recur as long as the original cause of stasis or ischemia remains uncorrected. This oversimplification of the pathology of indolent ulcers serves to emphasize the fact that the cause of the ulcer must be removed if a permanent cure is to be effected. It is beyond the scope of this paper to consider in detail the pathology of indolent ulcers. The reader is referred to a recent article by Heller<sup>1</sup> for an excellent pathologic description.

A frequent error is to treat the ulcer and forget its owner. The proper management of these cases requires a complete and careful history and physical examination, including a blood count, urinalysis, and blood serology. Other laboratory work and special examinations should be done when indicated.

In taking the history, special attention should be given to such matters as pain upon use of the limb, numbness and coldness of the toes, discoloration of the skin, a history of thrombosis, and frequency of recurrence of ulceration. Answers to these queries may lead to the diagnosis of other vascular diseases such as Buerger's or Raynaud's disease or arteriosclerosis.

In the local examination of the extremity, the examiner should observe skin changes, evidence of venous stasis, the character of the pulse in the dorsalis pedis, posterior tibial, popliteal, and femoral arteries. If veins are observed, the Trendelenburg and Perthes tests should be done. An attempt should be made to elicit Homans' sign.

**Fluorescein Dye Tests**—Skin temperature tests and fluorescein dye tests are especially helpful in those cases where ischemia and stasis appear together, as well as to determine the condition of circulation in the skin around the ulcer.

site. We have found the fluorescein dye test as dependable as either skin temperature or oscillographic determinations. Also, it gives more accurate information as to the level of arterial involvement and the character of capillary circulation in the skin.

Ten cubic centimeters of a 5 per cent intravenous solution of fluorescein dye and a mercury lamp make up the special equipment for this test.<sup>2</sup> The lamp has a glass filter which excludes most of the light rays and transmits light only in the region of 3,600 angstrom units. The dye is slowly injected intravenously. In fifteen to twenty seconds, depending on the speed of the patient's circulation, all areas exposed to the lamp rays where the circulation is good will show an intense golden green hue. It becomes more intense as more of the dye diffuses from the capillaries into the tissues. Cross scratches on the leg make fluorescent lines showing levels to which good circulation travels. Tissue with poor circulation shows as a dark purple color contrast.

In our opinion there are very few contraindications to surgery in ulcer cases. Age is certainly not one of them. We have operated successfully on a number of patients over the age of 70 years and on a few past 80. If concomitant constitutional disease such as diabetes, tuberculosis, or decompensated cardiac disease is found, we delay surgery until these diseases are in check. Otherwise they are treated much the same as any other patient. We do not operate in the presence of serious infection, anemia, or malnutrition. We believe that surgery usually should not be done during pregnancy.

*Local Treatment as an Adjunct*—Since most leg ulcers are infected, local treatment must be instituted before surgical procedures are possible. Local treatment has only three purposes—to relieve pain, to combat infection, and to relieve congestion and thereby promote healing. While local treatment will not eradicate the cause of ulceration, it is a necessary adjunct to surgical management, especially to clear up an infected ulcer so that surgical procedures can be used.

Infection is usually due to low-grade staphylococci, streptococci, *Bacillus subtilis*, aerobic spore formers, and epidermophytids. To overcome these infectious organisms we have found that a solution of gentian violet painted on the ulcer combined with a light dusting with sulfathiazole crystals cleans up the ulcer faster than any other method we have tried. Gentian violet has been proved by Holmes and Wilson<sup>3</sup> to be bacteriostatic to the group of organisms mentioned previously as being the usual infective agents.

One of us<sup>4</sup> in 1940 first advocated the local use of sulfonamide drugs in this type of ulcer. Our clinical experience during the past seven years has confirmed our opinion of the value of this combination in infected ulcers.

We cannot agree with those who condemn the local use of sulfonamide compounds in such infections. The recent reports of More<sup>5</sup> and Meloney<sup>6</sup> confirm our belief. In ulcer cases especially, the systemic use of this drug is not as efficacious as its local application because the local blood supply is impaired. We restrict the use of sulfathiazole to infected ulcers and discontinue local application as soon as infection has subsided. Poseh and associates,<sup>7</sup> in experimental studies at Wayne University, established that sulfonamide drugs are

local irritants to the dermis and subcutis but stated that such undesirable effects can be minimized by the use of small amounts of the drug in micro-crystalline form. We too have observed that the prolonged use of the drug inhibits epithelialization.\*

**Pressure Dressings**—When stasis is present in the leg, as it usually is in such ulcers, its control by Unna's paste boot, cotton elastic bandage, elastoplast, or some other form of pressure dressing is essential to promote healing. McPheeters<sup>10</sup> was among the first in this country to advocate the use of a rubber sponge with a cotton elastic bandage for this purpose. We have modified his method somewhat by using a soft sponge rubber one-half inch thick in place of the commercial rubber bath sponge. Sponge rubber can be purchased by the yard and cut to fit the size ulcer being treated. Used with the cotton elastic bandage, it supplies constant pressure to the ulcer, exerts a gentle stimulation to the ulcer bed, improves the circulation, prevents venous stagnation, and absorbs the exudate. When pruritis is a factor, x-ray exposure to the back by the technique used in lichen planus, gives gratifying relief by its effect on the sympathetic nerves.

Tables I and II serve to demonstrate the value of pressure dressings in hastening the healing of leg ulcers. The local treatment consisted of the application of gentian violet solution and sulfathiazole crystals. In the varicose type, vein ligations were done routinely.

This series is too small to warrant conclusions as to the comparative value of Unna's boots and sponge rubber as pressure dressings. However, it should be noted that in five instances sponge rubber dressings effected healing after adequate trials with Unna's boots had failed. In two cases where sponge rubber failed, deep phlebotrombosis was present requiring femoral vein ligation.

The principal advantages of sponge rubber over Unna's paste boot are its ease of application, saving of time, and its absorptive powers. Thus, it lends itself to office practice where time is so often a deciding factor in the choice of dressings. Moreover, unless Unna's boots are skillfully and accurately applied they are not only useless but detrimental to the patient. Very little skill is required to fit and apply the sponge rubber dressing.

In varicose ulcers, which are by far the most numerous type encountered, the underlying cause is the varix that feeds them. Therefore, we believe that as soon as infection in the ulcer is under control ligation of all varicosities should be done. To us this means that the greater saphenous vein and all branches found near the fossa ovalis must be separately ligated, and that all "blowouts" in the thigh or leg should likewise be ligated.

Usually following such ligation and subsequent injection of any remaining varicosities with sclerosing solution, the ulcer shows marked improvement. If after these procedures have been properly done, the ulcer persists, a careful

\*Since submission of this article for publication we have been using a new soluble dressing containing a nitrofurantoin compound in the local treatment of infected ulcers. This dressing is bactericidal and bacteriostatic to most skin organisms even in high dilutions. It is relatively nonirritating and does not retard tissue repair. Therefore, we believe it is an improvement over the local use of sulfonamides.

TABLE 1. UUNA'S BOOT PRESSURE DRESSING

CASE	AGE (IN YR.)	SIZE OF ULCER (IN CM.)	WEEKS OF TREAT- MENT	TYPE OF ULCER	RESULTS	REMARKS
W. F.	64	1 x 1½	4	Varicose	Healed	
B. S.	69	3 x 3 ½ x 1	3	Ischemic and varicose	Healed	Recurrence in 2 months
H. T.	79	5 x 8	20	Ischemic	Healed	Recurrence in 6 weeks, then treated with sponge rubber with complete healing in 6 weeks
J. E.	33	2 x 3	12	Varicose	Healed	Ulcer recurred 3 times in 6 years; next recur- rence should have skin graft
H. L.	34	2 x 3	16	Varicose	Slight improve- ment	Is a controlled diabetic; healed in 3 weeks with sponge rubber dress- ings
K. V.	42	3 x 4	125	Varicose	Slight improve- ment	Healed in 9 weeks with sponge rubber dress- ings
C. W.	81	1 x 2	24	Ischemic	No improve- ment	Healed in 6 weeks with sponge rubber dress- ings
L. S.	53	1 x 5½	13	Varicose	No improve- ment	Healed in 8 weeks with sponge rubber dress- ings
J. P.	32	2 x 3	6	Varicose	Healed	
A. B.	54	2 x 4	8	Varicose	Healed	
V. R.	42	1 x 2½	4	Varicose	Healed	
L. A.	69	3 x 4	12	Ischemic and varicose	Healed	
L. C.	43	1 x 2	4	Varicose	Healed	
B. F.	53	1½ x 3	7	Varicose	Healed	
B. B.	51	2 x 2	6	Varicose	Healed	
F. C.	43	2 x 2½	8	Varicose	Healed	
E. G.	43	1½ x 2	6	Varicose	Healed	
C. L.	44	2 x 2	6	Varicose	Healed	

investigation of the area about the ulcer must be made. It may be found that some degree of arterio- or arteriolar sclerosis exists. Skin temperature and fluorescein dye tests are helpful in this determination. Or the ulcer may be situated over a pool of varicosities into which an incompetent perforating branch from the deep system is feeding deoxygenated blood. In some cases scar tissue surrounds the ulcer and interferes with the blood supply. Most often the cause of nonhealing of the ulcer in the face of adequate treatment of the associated varicosities will be found in the poor type of epithelial tissue being formed from the ulcer margins.

*Plastic Operations*—In cases where arteriosclerosis and venous stagnation are both present physiotherapy is of benefit. Where "blowouts" occur under the ulcer bed and where dense scar tissue surrounds the ulcer area, we resort to plastic operations on the ulcer. For this we employ a modification of the Kondoleon operation. An elliptical incision is made around the ulcer including within the ellipse the scar tissue. The incision is carried down to the deep

TABLE II. SPONGE RUBBER PRESSURE DRESSINGS

CASE	AGE (IN YR.)	SIZE OF ULCER (IN CM.)	WEEKS OF TREAT- MENT	TYPE OF ULCER	RESULTS	REMARKS
L. K.	64	1 x 1½	4	Varicose	Healed	A controlled diabetic Moderate arteriosclerosis of leg Moderate arteriosclerosis of leg 15 weeks with Unna boot, no improvement
H. L.	51	1 x 1	3	Varicose	Healed	
C. W.	81	1 x 1½	6	Ischemic	Healed	
H. T.	79	1 x 1	6	Ischemic	Healed	
L. S.	58	1 x 4	8	Varicose	Healed	
M. A.	38	2 x 2	8	Varicose	Healed	12½ weeks' treatment with Unna boots and various locally ap- plied drugs with only slight improvement
K. M.	42	2 x 3	9	Varicose	Healed	
A. T.	66	2 x 3	11	Ischemic and varicose	Healed	Chlorophyl penicillin ointment used locally, first healing in 10 years
M. L.	55	3 x 4½	14	Varicose	Improved	Deep phlebotrombosis, femo- ral ligation and skin graft done before complete healing
M. H.	62	2½ x 3	10	Varicose	Healed	Recurrence in one month, re- quired skin graft
C. S.	52	6 x 9 5 x 8 5 x 8	11	Varicose	Improved	Required femoral vein ligation and skin graft to effect heal- ing because of deep phlebo- thrombosis
H. C.	29	2 x 2½	11	Trophic	Improved	Skin graft necessary to effect healing
J. M.	71	1½ x 6 2 x 4	20	Ischemic	Improved	Last 8 weeks of treatment, chlorophyl penicillin ointment used with excellent response; skin graft done to effect com- plete healing
S. N.	67	3 x 3	12	Ischemic	Healed	Cardiac obesity, 330 pounds
R. K.	54	5 x 8 2 x 3	12 4	Ischemic	Improved	
L. O.	34	2 x 3	3	Varicose	Healed	
S. B.	64	3 x 3	6	Ischemic	Healed	

*fascia* If there are any varicosities feeding the ulcer, they are ligated as encountered. The scar tissue and ulcer are then excised and the wound is allowed to form healthy granulations which are skin grafted. We have tried less extensive operations such as excising the scar tissue on each side of the ulcer and sliding a full-thickness pedicle graft over the ulcer. In our hands this procedure has not been as successful as complete removal of the entire ulcer and scar tissue.

This extensive plastic operation is necessary only in those few cases where long-standing or repeated ulceration has built up a thick cicatricial periphery. In most instances we have found that failure to heal completely has been due to the presence of poor epithelial tissue. This is particularly true where the ulcer measures 3 cm. or more in diameter. These larger ulcers tend to form a very thin, avascular type of epithelium. Skin grafting such ulcers, once healthy granulation tissue has formed, not only lessens the period of disability by weeks but also affords the best insurance against recurrence.

In Table III is illustrated the value of skin grafting in long-standing or recurrent ulcers. While one lesson to be learned from these cases is that skin

TABLE III SKIN GRAFTED CASES

CASE	AGE (IN YE.)	DURA TION OF ULCER (IN YE.)	SIZE OF ULCER (IN CM.)	WEEKS OF TREAT- MENT	TREATMENT	RESULT
M. L.	53	15	$2\frac{1}{2} \times 2\frac{1}{2}$	3	Femoral vein ligation followed by pinch graft	Healed
C. S.	52	12	$5 \times 7$	5	Femoral vein ligation followed by pinch graft, saphenous ligations previously done and skin graft failed	Healed
H. C.	29	2	$2 \times 2$	4	Atrophic ulcer with good arterial and venous circulation, all other forms of treatment failed, skin graft was done in out patient de- partment and patient remained ambulatory	Healed
J. M.	71	$8\frac{1}{2}$	$1\frac{1}{2} \times 1\frac{1}{2}$ and $1\frac{1}{2} \times 2$	2	Ulcer, originally $12 \times 18$ cm., re- duced in size by pressure dress- ings, finally reached a static stage when pinch grafts were applied	Healed
M. H.	62	5	$2\frac{1}{2} \times 7$	7	Recurrent ulcer which failed to re- spond to local treatment until skin graft was done	Healed
E. A.	62	34	$2\frac{1}{2} \times 2\frac{1}{2}$	6	Plastic excision of ulcer first done because of scar tissue with skin graft delayed until new granula- tion formed, preliminary high saphenous vein ligation	Healed

grafting will effect a cure when all else fails, a much more important deduction is that the patient can be saved months and years of suffering and disability when large or recurrent ulcers receive early skin grafting

*Pinch Grafts*—Preliminary to skin grafting of ulcers we believe that all varicosities should be adequately treated by ligation and sclerosis, the ulcer bed must be free of infection, the skin circulation must be adequate as determined by fluorescein dye tests and avitaminosis, hypoproteinemia and anemia, if present, must be corrected

The most successful skin graft method judged by the percentage of takes, time of donor and recipient areas to heal, and comfort to the patient is the pinch or Reverdin type. Two per cent novocain infiltration anesthesia is used. The anterior or lateral thigh is selected as the donor site. Small thin pinch grafts are removed from a prepared area dipped into plasma and then planted, cut surface down into the clean granulation tissue of the ulcer over which thrombin topical solution has been applied. This coagulates the plasma and sticks the grafts more securely in place. The donor and recipient areas are then covered by coarse mesh paraffin gauze, petrolatum gauze, fluffed plain gauze, a cotton pad, and bandaged with a cotton elastic bandage as a pressure dressing. Both areas are dressed on the seventh or eighth day. The "takes" have been well above 90 per cent in all cases and remained successful in all but one. In this case the grafts remained until the patient was ambulatory for two weeks. Then they gradually sloughed away because of poor circulation shown by tests. The grafts were repeated two weeks after a femoral vein ligation and they are successful after four months of ambulation.

When dealing with leg ulcers in patients who give a history of an old deep phlebothrombosis, it is often impossible to improve the circulation by the usual methods. As a result ulcers in such cases are hard to heal. We have found that ligation of the femoral vein below the profunda as originally advocated by Homans<sup>9</sup> and later by Collier and Buxton<sup>10</sup> improves the circulation considerably and permits the successful skin grafting of the ulcer site. We do not follow Homans' advice regarding not ligating the saphenous vein. We ligate both the saphenous and the femoral veins and have found it very helpful to the patient. Except for some temporary cramping and a slight degree of swelling lasting for several months, we have noted no untoward aftereffects.

#### SUMMARY

1. A careful history and physical examination with special attention to signs and symptoms of other peripheral vascular diseases is necessary to determine the cause of leg ulcers.

2. Fluorescein dye tests have proved helpful to determine the condition of the circulation around the ulcer site. This test is more easily performed than skin temperature and oscillometric determinations and yields almost as much information.

3. Local treatment is a necessary adjunct to surgical management. In our experience the most useful local treatment has been gentian violet solution, sulfathiazole crystals, and compression bandages of sponge rubber.

4. Surgical correction of ulcer causative factors should follow as closely as possible the local treatment of the ulcer. Surgical measures include vein ligations, plastic operations on old ulcers, and skin grafting of larger ulcers, as indicated in each case.

5. The authors' technique for skin grafting is described.

6. The results of pressure dressings with Unna's paste boot and sponge rubber in thirty-four cases is presented in tabulated form.

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## A SIMPLE DEVICE TO TEST AND TO IMPROVE THE CIRCULATION IN A PEDICLE FLAP

HANS MAY, M D, PHILADELPHIA, PA.

**I**N CONSTRUCTING and transplanting a pedicle flap, aside from certain general rules, such as selecting the proper donor area, outlining the flap, allowing for shrinkage, and cutting the flap of equal thickness, a sufficient arterial and venous circulation in the flap is of utmost importance. A flap, with a broad pedicle and not longer than twice the width of the pedicle and the flap lying along the axis of the circulation of the donor area, can as a rule be immediately transferred. In long narrow flaps, however, and those crossing the long axis of the circulation of the donor area, transfer should be delayed for the purpose of securing an adequate blood supply. There are, however, cases in between these two extremes, where the question as to immediate or delayed transfer can be answered only by testing the circulation of the flap. An accurate test of the blood supply of a flap is also helpful whenever a flap must be severed from its pedicle or whenever a double pedicle flap is to be converted into a single pedicle flap. There are various ways of testing the circulation as, for instance, the temperature return test of Douglas and Buchholz, and the fluorescein test of Dingwall and Lord. I found the method to be described here simple and versatile. As a matter of fact, it is so simple that it may have been used by others. However, as far as can be ascertained, it has not been described in literature as yet.

The test is made by means of an ordinary laboratory clamp. The clamp, however, should be of the type depicted in Fig 1, that is, it should be closed on all four sides. The lower crossbar, however, should be rotatory so that it can be swung open like a door. The clamp is attached to that pedicle of a flap which needs to be severed. The clamp is applied as follows. The crushing bar of the clamp is raised by turning on the thumb screw. The lower bar is open. The pedicle of the flap is inserted into the space below the crushing bar. The lower bar is swung back in place, thus closing the space in which the pedicle lies. The pedicle is now gradually clamped by setting up on the thumb screw until the color of the flap changes. It is then possible to determine the adequacy of the circulation. The tip of the finger is pressed upon the flap near the clamp for a few seconds; this leaves an anemic mark which, if the circulation is adequate, returns to normal immediately. If the return to normal color is slow, or absent, the pressure of the clamp is lessened by turning the thumb screw in the reverse way. If the crushing causes pain, a few cubic centimeters of novocain should be injected into the pedicle.

The great advantage of this test is its accuracy and simplicity of application. Also, the clamp is not bulky. A few examples will demonstrate the versatility of the method.

The laboratory clamp test may be applied to an open pedicle flap. The open pedicle flap as distinguished from the tube flap can be used whenever a direct approach of flap and host area can be accomplished, no matter whether the flap is transferred to the host area or the host area to the flap. Whenever the length or location of a flap is such as to cast doubt concerning the adequacy of its circulation, the flap is raised between two parallel incisions and left attached temporarily at two pedicles (bridge flap). The pedicle, which is to become the peripheral end of the flap, is clamped with an elastic intestinal clamp. If the color of the flap does not change, this pedicle of the flap can be severed and the flap transferred immediately. If the color changes, transfer should be

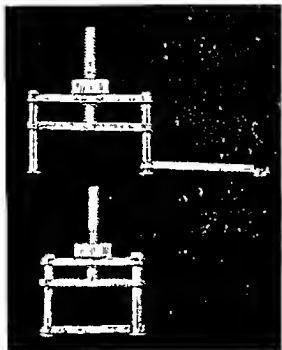


Fig. 1—A medium-sized and small laboratory clamp. The lower crossbar is rotatory so that it can be swung open like a door.

delayed and the circulation improved by application of the laboratory clamp to the peripheral pedicle of the flap. The latter is narrowed by incising it from either side for one-third of its distance, leaving the middle third preserved. The laboratory clamp is now attached to the middle third and all wound edges are sutured together. The following day gradual crushing of the narrowed pedicle is begun by tightening the clamp. After each tightening the adequacy of the circulation is tested as just described. After the pedicle is crushed completely, the clamp can be removed and the flap may be ready for transfer, unless the crushing has caused edema in the flap. If this is the case, transfer should be delayed until all edema has subsided. Immediate application of the laboratory clamp may be inadvisable in flaps which show marked change of color



Fig. 4. A-C—4. Patient, aged 46 years, referred for closure of a full thickness defect of the left cheek after irradiation of cancer. Frequent biopsies were negative. A cervical tube flap was constructed reaching from the left mastoid region to the clavicle. Three weeks later the flap was lengthened. This part of the flap was left untubed and returned to its original site. Two weeks later it was elevated again. The peripheral pedicle narrowed from either side and the laboratory clamp attached to the remainder of the pedicle. The pedicle was gradually crushed within five days. *B* Four weeks later the peripheral edge of the untubed flap was raised and lined by folding it upon itself. The flap bed was skin grafted. *C* Three weeks later the communication of covering and lining of the flap, that is the peripheral edge of the flap, was incised. One week later the flap was sutured into the defect. Ten days later the pedicle was gradually crushed with a laboratory clamp. This took four days when the flap could be severed from the pedicle and adjusted in place.

upon application of the intestinal clamp. If this is the case, the flap should be returned to its original site and sutured in place. After three weeks the flap is raised again and the laboratory clamp is applied as described. After the pedicle is crushed one should wait until all edema has subsided before transferring the flap. As a matter of fact, in some instances where the circulation was particularly poor, another raising and returning of the flap—the flap now being a single pedicle flap—may be advisable (Figs. 2 to 4).



Fig. 4 D and E—Patient one year after operation

After the transfer of the flap, the laboratory clamp method is again useful in separating the flap from its pedicle. It is also applicable to tube flaps. The skin at the site of the crushing of the tube flap, however, should be incised all around the tube, rendering the area more pliable and less painful.

#### SUMMARY

With the aid of an ordinary laboratory clamp, which is closed on all four sides but has a rotatory lower crossbar, it is possible to test and to improve the circulation in a pedicle flap. Several examples are depicted, which demonstrate the method.

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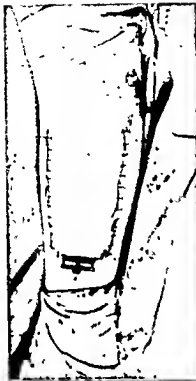


FIG. 2.—A, Patient, aged 54 years, referred to us for treatment of a deep decubital ulcer of right heel from pressure of plaster cast. The original incision, extending to the right leg 30 cm. from the heel, was closed with a flap raised from the lateral aspect of the leg. The flap was returned to its original site. After six weeks the flap was raised again, its peritibial border margined one-third from either side. A laboratory clamp was applied to the midline, and the flap returned to its original site. The peritibial border was gradually crushed within five days and the clamp removed. Two weeks later all edges had disappeared from the flap. The flap was raised again. The peritibial edge, however, became discolored, brown, flat, and was returned once more to its original site. This week later the flap was raised. The area from which the flap was raised was skin grafted. The ulcerated area at the right heel was excised, the flap leg removed, and the flap sutured into the defect. In the leg were immobilized in a plaster cast. Seven days after the laboratory "flap" was applied to the foot, the heel was anatomically crushed with a laboratory clamp. The flap was held in place by a laboratory clamp. The heel was anatomically crushed with a laboratory clamp. At the time of the first operation, as well as the time of the second, the flap at the heel, were adjusted in place. Wound healing was excellent.

B

C

D



D

C

Fig. 3—A. Patient with extensive scarring ulceration and sequestration over left tibia from osteomyelitis. B. A large double pedicle flap was raised at the right thigh. First the upper half was mobilized between two parallel incisions and returned to its original site. Two weeks later the entire flap was mobilized and returned to its original site. Two weeks after this the flap was elevated again, the peripheral pedicle was narrowed, and the flap was returned to its original site. C. Two weeks later the flap was again raised. The peripheral end became discolored and the flap was again returned to its original site. The log was removed, and the flap sutured in place after the flap had been skin grafted. Ten days later the pedicle of the flap was narrowed from either side and the laboratory clamp applied to the middle section. The remainder of the pedicle was gradually clamped within one week. The cast was removed. Three weeks later the flap was adjusted in place. D. Patient three months after operation.



Fig 1 A-C—A, Patient aged 46 years referred for closure of a full thickness defect of the left cheek after irradiation of cancer. Frequent biopsies were negative. A vertical tube flap was constructed reaching from the left nasal region to the clavicle. Three weeks later the flap was longitudinal. Thin part of the flap was left attached and returned to its original site. Two weeks later it was elevated again, the peripheral pedicle narrowed from either side and the laboratory clamp of the pedicle attached to the remainder of the pedicle. The pedicle was gradually crushed within five days. B, Four weeks later the peripheral edge of the tubular flap was raised and lined by folding it upon itself. The flap had now skin grafted. C, Four weeks later the reconstruction of covering and lining of the flap, that in the tubular edge of the flap, was lifted. One week later the flap was sutured into the defect. Ten days later the pedicle was gradually crushed with a laboratory clamp. Thin took four days when the flap could be sutured from the pedicle and adjusted in place.

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D E  
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## THE TREATMENT OF SUPERFICIAL PYOGENIC INFECTIONS BY THE DIRECT INJECTION OF PENICILLIN

LIEUTENANT COLONEL JOHN M. KENNY, MEDICAL CORPS,  
ARMY OF THE UNITED STATES

FOR the past eighteen months I have been treating superficial pyogenic infections by the daily injection of a penicillin-novocain mixture directly into the involved tissues. It has been observed that after one or two such treatments pain and redness usually disappear, and that after five or six injections all evidence of infection is usually absent and the healing process well established. In fact, the response of the infections thus treated has been so rapid and satisfactory that it suggests that this method of treatment may be superior to the orthodox methods such as heat, rest, elevation of the affected part or the systemic administration of sulfonamide derivatives or penicillin. At my suggestion several other medical officers have also followed this procedure and have been equally successful. Because of lack of facilities it has not been possible to review exhaustively the literature on penicillin, but it is my impression that the technique to be described has not been previously published.\*

The solution used was made by dissolving 100,000 units of penicillin in 100 c.c. of normal saline and adding 100 c.c. of 1 per cent novocain, the final strength being 500 units per cubic centimeter in 0.5 per cent novocain. This strength of penicillin was selected because it had previously been found to be nonirritating to the eye† and should therefore be nonirritating to other tissues. The novocain was added to minimize the pain associated with the injection of penicillin into an inflamed area. The patients were all Army personnel with some type of an acute infectious process involving the skin and subcutaneous tissues.

If pus was present the skin was infiltrated with the mixture, incised, and gross slough removed. The area of obvious inflammation and a 1 to 4 cm. band of surrounding normal tissue were then heavily infiltrated with the solution, from 15 to 150 c.c. of solution being used depending on the size of the lesion. This was done by beginning at the periphery and working toward the lesion. As a final step the center of the lesion was infiltrated through the abscess wall, if present, to insure a high concentration at the point of maximum injection. By starting at the periphery, the possibility of forcing organisms out into uninvolved tissues is avoided. It is to be emphasized that several of the rules for handling infected tissues were grossly violated in that (1) injection of the solution was made directly into infected tissues by passing the needle through the walls of abscess cavities or through inflamed skin,

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\*After this manuscript had been completed an article was found which described a similar technique. Rose, D., and Hurwitz, D. The Regional Injection of Penicillin in Local Infections, New England J. Med. 234: 291, 1946.

†Morris, Frank O'N. Personal communication.

(2) infected tissues were grossly distended with the solution to insure a heavy concentration of penicillin in and around the area of infection, and (3) frequently no attempt was made to put the involved area at rest. Injections were repeated each twenty-four hours until all evidence of infection had disappeared, a matter of three to seven days. Supplementary therapy was omitted except in a few cases in which heat, rest and elevation of the affected part were used. The use of sulfonamide derivatives or penicillin systemically was avoided.

Bacteriologic studies were attempted on a number of the patients treated. However, due to the inexperience of the laboratory personnel, isolation of various strains of organisms was unsatisfactory. Frequently the reports, such as *Sarcinia*, suggested contamination of the cultures. Therefore, it is not possible to report on this aspect. Clinically the causative organism in all cases, except the patients with Vincent's infection, appeared to be some strain of streptococcus or staphylococcus.

A brief description of the various types of lesions treated and the results obtained follows:

1. *Carbuncles*.—There were four cases of carbuncles, two on the dorsum of the hand, one on the neck, and one on the back, varying in size from 5 to 12 cm. in diameter. These were in the suppurative stage when first seen and at the time of the initial injection cruentate incisions were made and slough removed, but no tissue was excised. From 100 to 150 c.c. of penicillin solution were injected daily for five to seven days. At the end of this time there was no evidence of infection and healing had begun. There was no supplementary therapy; two patients were treated on an ambulatory basis. The striking feature in each case was the very rapid subsidence of pain, swelling, and redness, within twenty-four to forty-eight hours, and the early appearance of the healing process. It was estimated that complete healing occurred in about two-thirds the time ordinarily to be expected with orthodox methods of treatment.

2. *Vincent's Infection of the Tonsils*.—There were three cases of Vincent's infection of the tonsils. Each patient had been proved resistant to all the usual forms of treatment, including large amount of systemic penicillin, and had had either several rapid recurrences or else a long period of hospitalization without improvement. The peritonsillar tissues were injected with 20 to 30 c.c. of solution each day for from five to seven days, with complete subsidence of all infection. There were no recurrences during a three-month follow-up period. The results obtained in these cases are considered highly significant because each patient had a chronic infection which for a long period of time had been resistant to the common methods of treatment.

3. *Miscellaneous Skin Infections*.—There were seventy-two miscellaneous skin infections, including boils, furuncles, cellulitis, etc. These were the common run of skin infections—boils with and without cellulitis, furuncles of the arm or leg, infected sebaceous cysts, cellulitis of the dorsum of the foot and ankle secondary to trichophytosis, cellulitis of the hand or arm secondary to cuts or scratches, and so on. Some of these infections were on the face and several involved the nose, supraorbital or infraorbital area.

Depending on the size and severity of the infection, the patients in this group received from two to seven injections of penicillin of 15 to 50 c.c. each time. Usually there was prompt relief from pain, within twenty-four hours, and rapid subsidence of evidence of infection within forty-eight to seventy-two hours. Most of these patients were treated on an ambulatory basis and it is believed that many hospital days were saved by this therapy. It is also believed that those patients who were hospitalized were returned to full duty much more rapidly than they would have been had they been treated by the more conventional methods of heat, elevation, and rest to the affected part, or by systemic sulfonamide or penicillin.

4 *Hand Infections*.—Several felons and paronychia were treated by this method in each instance after establishing adequate drainage. Rapid subsidence of infection was noted.

5 *Pilonidal Cysts*.—There were twenty cases of pilonidal cysts. The preparation was used in two different ways in these cases. *Acute abscesses* were treated as described under Miscellaneous Skin Infections. However, if it was decided to excise the cyst the injections were continued for a total of ten days, at which time the area was usually suitable for excision and primary closure, provided the method to be described later was followed. *At operation*, after excision of the cyst and its sinus tracts and after mobilization of sufficient surrounding tissue to permit primary closure without tension, all the tissues in the area of excision and mobilization, especially the fat, were heavily infiltrated, using from 200 to 300 c.c. of penicillin. The solution contained no novocain in this instance. Twelve cases were handled in this manner with primary union and no drainage of any kind, in each instance.

6 *Deep Infections*.—One patient had a *chronic infection of the submaxillary salivary gland*. This patient had had repeated episodes of an acute inflammatory nature which had required drainage. When first seen he was in an acute exacerbation of the infection. Drainage was established and the infected tissues were infiltrated daily with penicillin. Ten days later the gland was excised, the wound infiltrated with penicillin, and closed without drainage. There was primary union. One patient with *acute axillary abscess* had a past history of a similar infection which had been quite stubborn and had required repeated incision and drainage. Drainage was established and the axilla infiltrated daily with about 75 c.c. of solution. There was early subsidence of infection and no recurrence. One patient had a *chronic draining axillary sinus tract* following drainage of a deep axillary abscess. A ten-day period of daily injections of the axilla with penicillin failed to stop drainage. The tract was dissected out and found to terminate in a partially destroyed lymph node. The operative wound was thoroughly infiltrated with penicillin and the wound closed without drainage. Healing was by primary intention.

7 *Contaminated Wounds or Operative Fields*.—The preparation has been used as a local anesthetic in the treatment of a number of contaminated wounds such as are seen in accident cases, after fights and the like. The tissues involved were heavily infiltrated, carefully cleansed, and thoroughly debrided in the usual manner and closed primarily without drainage. There

were no infections. The same procedure was carried out in operative fields which were sites of known infections as has been previously described under Pilonidal Cysts and Deep Infections. Primary union without drainage was obtained in each instance.

#### DISCUSSION

It is a well-known fact that penicillin is normally only a very temporary guest of the human body, reaching its peak concentration about one hour after intramuscular injection, and being largely excreted within three hours. It is likewise known that while some bacteria are susceptible to this drug at the usual low concentration achieved in body tissues, others succumb only at higher levels than are attainable by systemic penicillin.

Because of these factors—low concentration, rapid excretion and variable bacterial susceptibility—frequent injections of large amounts of systemic penicillin for periods of four to ten days are usually required to control localized pyogenic infections such as those described in this paper. Furthermore, some pyogenic infections respond poorly or not at all to systemic penicillin. It was believed that if a method could be found whereby a very high local concentration of penicillin could be obtained, there might be more rapid subsidence of the infection, injections could be made at longer intervals, and some infections not amenable to systemic penicillin might be controlled. The direct injection of penicillin into the infected area was the only method which seemed to offer the possibility of obtaining the high local concentration desired. When this was done, injecting penicillin directly into the infected area, the results obtained indicated that the infection was usually controlled more rapidly, healing began earlier and it was completed faster than when comparable cases were treated with systemic penicillin. The most significant results were obtained in the three patients with Vincent's infection of the tonsil because this method succeeded where systemic penicillin had failed. These observations lead to the belief that many localized infections which respond slowly or not at all to systemic therapy can be treated successfully and more rapidly by the local injection of penicillin.

The solution used was weak, 500 units per cubic centimeter, and was deliberately chosen to minimize the tissue irritant effect of the drug. There is no logical reason why higher concentrations should not be used, except that this may lead to more residual soreness after the effect of the novocain has disappeared. This has been noted in a few cases in which solutions of 2,000 units per cubic centimeter have been used. However, in severe and spreading infections higher concentrations, up to 50,000 to 60,000 units per cubic centimeter, would certainly seem best. The twenty-four hour interval between injections, while satisfactory in the patients treated, is entirely arbitrary and in more severe, or in spreading infections, injections at twelve-, eight- or even four-hour intervals are probably desirable.

It is to be emphasized that the usual rules of providing drainage for accumulations of pus must be followed. However, it is believed that the surgery can be more limited, as in carbuncles where excision of tissue was not found to be necessary.

Of particular interest are the results obtained by using it to infiltrate the contaminated wound seen in accident cases, or the definitely "dirty" operative field such as is found after the excision of pilonidal cysts. When the tissues of such wounds were heavily infiltrated, they were closed without drainage and no infection developed. This opens a wide field of use and may well make possible the carrying out of extensive procedures in infected or contaminated fields, which heretofore were dangerous because of the high incidence of postoperative wound infection. The closure of colostomies and fecal fistulas are examples of such cases.

This method of therapy also eliminates the need of frequent injections of penicillin and thus makes possible the ambulatory treatment of many patients who would otherwise have to be hospitalized. It is also my impression that the infections so treated have cleared up more rapidly than have similar ones treated by heat, rest, elevation, and the systemic administration of sulfonamide derivatives or penicillin. They have therefore resumed normal activities at an earlier date. Both of these factors are of considerable economic importance to the average patient.

#### SUMMARY

Approximately 100 patients with pyogenic infections of the skin and subcutaneous tissue have been treated by the direct injection into the involved tissues of a mixture of penicillin and novocain. In all cases the infection subsided rapidly, and in most cases it appeared to subside more rapidly than did comparable cases treated by heat, rest, elevation, or the systemic administration of sulfonamide derivatives or penicillin. There were no failures and no complications. Three cases of Vincent's infection of the tonsil which had been resistant to all forms of treatment including systemic penicillin were cured by the local injection of penicillin.

In fourteen operations in contaminated fields, as in excising a pilonidal cyst, the wound was infiltrated with penicillin and closed without drainage. There were no postoperative infections.

#### CONCLUSIONS

1. The direct injection of penicillin in superficial pyogenic infections is a safe and practical method of treatment.

2. Infections so treated responded as rapidly as, or more rapidly than, similar infections treated in the orthodox manner with heat, rest, elevation, or the systemic administration of sulfonamide derivatives or penicillin.

3. Some infections which cannot be successfully treated by, or which respond very slowly to, systemic penicillin can be treated rapidly and successfully by injecting penicillin directly into the infected tissues.

4. Contaminated operative wounds can be closed without drainage and without fear of postoperative infection, if the tissues are heavily infiltrated with penicillin.

The author wishes to express his gratitude to Major Frank O. N. Morris, and Captain F. W. James, Medical Corps Army of the United States, for their assistance.

## EFFECTS OF PROTEIN AND METHIONINE ON NITROGEN BALANCE OF BURNED RATS

ALFRED CHANUTIN, PH D., AND STEPHAN LAIDEWIG, PH D.  
CHARLOTTESVILLE, VA

(From the Biochemical Laboratory, University of Virginia, School of Medicine)

IT IS well established<sup>1</sup> that the urinary nitrogen excretion is markedly increased after thermal injury. Evidence presented by Croft and Peters<sup>2</sup> (1945) indicates that the loss in urinary nitrogen of burned rats is substantially reduced by the incorporation of 1 per cent methionine in the diet. The suggestion is made that the negative nitrogen balance or "the apparent toxemia is in reality a deficiency, induced by a call for one amino acid with consequent raiding of a whole protein molecule." It was felt that the importance of such a hypothesis warrants further investigation of this problem.

### METHODS

Male rats, 70 days of age, were used. The experimental diets are listed in Table I.

One gram of the following mixture was added to each 99 Gm. of diet:

Thiamine	20 mg
Vitamin K	4 mg
Pyridoxine	20 mg
Para amino benzoic acid	50 mg
Nicotinic acid	100 mg.
Calcium pantothenate	280 mg
Choline chloride	5,000 mg

These materials were dissolved in 100 cc of 20 per cent ethanol, and a 1 c.c. aliquot was added to each 100 Gm. of diet. Proper amounts of vitamins A, D, and E were fed as supplements twice weekly.

The animals were fed the respective diets for at least one week in stock cages before being placed in the metabolism cage. The food cups in the metabolism cages, which were equipped with removable metal collars, were placed within glass containers to prevent the scattering of food. The food intake was measured daily to the nearest gram. Tap water was always available in a water fountain. The animals rested on the screened bottoms of the cages. The metal funnel under the cage was coated with paraffin and the urine was collected daily in a graduate containing 5 cc of dilute  $H_2SO_4$ . The funnel was washed with water each day and the washings collected. The urine volume was measured and brought to 200 cc with the washings and distilled water, and aliquots were analyzed for nitrogen by the Kjeldahl procedure.

This work was done under contract with the Medical Division of the Chemical Warfare Service.

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TABLE I

DIET	I	II	III
Casein	20	20	40
Salt mixtures	4	4	4
Crisco	8	8	8
Sucrose	65	64	45
Agar	2	2	2
Vitamin supplement*	1	1	1
Methionine	—	1	—
Nitrogen analysis	2.92%	2.98%	5.92%

\*Vitamin supplement Sucrose, 195 Gm Inositol, 40 Gm, Riboflavin 0.1 Gm

Fecal contamination of the urine was prevented by using a fine screen at the bottom of the funnel

After anesthetizing the rats lightly with sodium pentobarbital, about one-third of the body surface was burned by dipping the clipped back in water at 75° C for sixty seconds. A hard crust formed over the burned area after a few days, and no "weeping" was encountered. An occasional animal died within a few hours after burning.

The first set of experiments (A) involved the feeding of the basal diet containing 20 per cent casein to twelve rats (I), the basal diet + 1 per cent methionine to twelve rats (II), and a diet containing 40 per cent casein to eight rats (III). This work was done during the summer months when the temperature in the laboratory was comparatively high. It was repeated (B) during the late fall months with Diets I and II (five rats for each diet) when the laboratory temperatures averaged about 22° C.

The standard error of the mean was determined by the formula

$$\sigma = \sqrt{\frac{d^2}{n(n-1)}}$$

in which  $d$  is the deviation from the mean and  $n$  is the number of animals. The statistical differences between means were calculated according to standard procedures.

#### RESULTS

The figure for nitrogen intake minus the urinary nitrogen was considered to represent the nitrogen balance. The fecal nitrogen determined for the control and burn periods was fairly constant and was not considered. It was found impossible to obtain a constant daily food intake and nitrogen output for the control period when the animals were allowed to ingest the food ad libitum. The nitrogen output varied daily for a given animal. Control periods were run from four to nine days in the A groups, and for seventeen days in the B groups.

The means and the standard errors of the means are used for the presentation of the data in each group. The data for both sets of experiments are shown in Table II.

The rats in group A weighed between 150 and 210 grams at the time they were placed in the metabolism cages. Their weights increased during the control period. After burning, most of the rats showed a slight decrease in

TABLE II. AVERAGE VALUES WITH STANDARD ERRORS OF NITROGEN BALANCE IN RATS<sup>\*</sup>

DIET	GROUP A						
	1	2	3	4	5	6	7
<i>Control Period</i>							
I (12) <sup>†</sup>	216 ± 14	173 ± 12	186 ± 16	156 ± 12	—	—	—
II (12)	166 ± 9	141 ± 11	143 ± 15	148 ± 11	—	—	—
III (8)	125 ± 38	175 ± 25	161 ± 26	258 ± 24	—	—	—
<i>Burn Period (Days After Burning)</i>							
I	-115 ± 13	-29 ± 31	-48 ± 25	4 ± 22	91 ± 19	126 ± 15	93 ± 19
II	-132 ± 18	-52 ± 32	-70 ± 33	88 ± 34	52 ± 40	110 ± 35	73 ± 24
III	-156 ± 34	-35 ± 26	53 ± 32	178 ± 75	22 ± 70	103 ± 31	143 ± 42
DIET	GROUP B						
	8	7	6	5	4	3	1
<i>Control Period (Days Before Burning)</i>							
I (5)	90 ± 14	131 ± 21	103 ± 5	99 ± 14	74 ± 22	124 ± 15	101 ± 11
II (5)	105 ± 14	111 ± 20	75 ± 16	121 ± 16	107 ± 19	131 ± 12	103 ± 32
<i>Burn Period (Days After Burning)</i>							
I	-86 ± 26	-115 ± 35	-44 ± 48	66 ± 10	0 ± 43	116 ± 20	47 ± 36
II	-116 ± 21	-51 ± 59	19 ± 23	15 ± 26	89 ± 18	164 ± 41	1 ± 51

<sup>\*</sup>Nitrogen intake nitrogen urinary excretion in milligrams<sup>†</sup>Figures in parentheses represent number of animals

weight which persisted during the period of observation. The animals in group B lost little weight during the burn period and in some cases tended to increase in weight.

In all cases the voluntary food intake markedly decreased from the control levels during the first two days after burning. In some animals the food intake remained below normal during the entire experimental period.

In group A (Table II) the mean values for "nitrogen balance" during the first four days of the control period were chosen as standards for comparison with the postburn period. The values on the first day for Diet I and the fourth day for Diet III are too high to conform with other control data. No statistically significant differences were noted in nitrogen retention during the control period except for the two values mentioned. It will be seen that there is a marked negative nitrogen balance immediately after thermal injury, which is apparently due to a combination of excessive nitrogen excretion associated with tissue destruction and to loss of appetite. Within a few days, the animals begin to ingest more food and retain nitrogen. A comparison of the mean values during the postburn period shows that there are no statistical differences between the basal, the methionine-basal enriched, and the high protein diets on any given day.

In group B, which was studied during cooler weather, the nitrogen retention was less than that observed for group A, which may be due to the difference in temperature. A comparison of the mean values for group B (Table II) during the control and burn periods shows no statistical differences between the data for nitrogen balance of rats on a basal and a methionine-enriched basal diet.

## DISCUSSION

Although the experimental procedures used in these experiments differ somewhat from those described by Croft and Peters, we were unable to con-



firm their findings. The English investigators fed definite amounts of a basal diet containing 10 per cent casein and 10 per cent dried yeast daily. The animals were withdrawn from the metabolism cages for three hours each day for feeding in order to avoid contamination of the urine samples. The urea and ammonia nitrogen alone were determined as a measure of nitrogen metabolism. In the present experiments, the rats were fed ad libitum, a twenty-four hour specimen of urine was collected, and total nitrogen was determined. Furthermore, these rats were burned at 75° C for sixty seconds in comparison with the exposure at 73° C for thirty seconds by Croft and Peters.

Several investigators have failed to confirm the findings of Croft and Peters.<sup>2</sup> Browne, Schenker, and Andreae<sup>4</sup> (1945) studied the nitrogen metabolism in patients suffering from thermal burns whose diets were supplemented with methionine. They found that the excretion of urinary nitrogen is not sufficiently affected after feeding this amino acid to warrant its use in burned patients. Abbott, Meyer, and Hirschfeld<sup>5</sup> studied the nitrogen excretion of burned dogs and were unable to note any significant difference in those animals receiving methionine over the control dogs.

#### SUMMARY

The intake and excretion of nitrogen in white rats fed on a 20 per cent casein basal diet, a basal diet supplemented with methionine, and a diet containing 40 per cent casein were determined before and after burning with hot water. During the first few days after thermal injury, all animals were in negative nitrogen balance. Neither the addition of methionine nor increased protein ingestion affected the retention of nitrogen significantly.

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## Case Reports

### PENETRATING HEART WOUND

#### THE REPORT OF AN INTERESTING CASE

MAJOR ROBERT W. ROBERTSON, MEDICAL CORPS, ARMY OF THE UNITED STATES

A PATIENT was wounded in the chest at 8:45 P.M. March 23, 1945, when an enemy machine gun bullet ricocheted off a stone wall. He was admitted to the 33rd Field Hospital, "B" Unit, at 11:15 with a sucking wound in the first interspace on the right side just lateral to the sternum. At that time the patient was cyanotic and respiration was difficult and painful. The sucking wound had been sealed airtight with a petrolatum gauze dressing. There was no other wound visible externally. The blood pressure on admittance was 120/20, the pulse 103 per minute, and the respirations were 30 per minute.

The preoperative radiographic picture of the chest showed a right hemopneumothorax with a mediastinal shift to the left (Fig. 1). A small foreign body the size of a split pea was present in the first interspace just to the right of the sternum. The radiographic picture of the pelvis on lateral view showed a bullet at the level of and just anterior to the lower border of the fifth lumbar vertebra. The anteroposterior view showed the bullet lying obliquely on the left side just medial to the sacroiliac joint (Figs. 2 and 3).

The patient was prepared for surgery by aspiration of 500 cc of blood from the right pleural cavity, the administration of 500 cc of blood intravenously, nasal oxygen, and 50,000 units of penicillin intramuscularly.

**Operation.**—An incision was made extending laterally and medially from the wound of entrance in the first interspace (anesthesia, gas [N<sub>2</sub>O] oxygen ether endotracheal). The anterior surface of the upper lobe of the right lung was seen to have a two inch laceration. As the lacerated area was being drawn laterally into the operative field a severe hemorrhage started from the mediastinal area. The whole pleural cavity seemed to fill with blood which was supposed to be originating from the pulmonary vessels or heart. The blood pressure immediately fell to zero. A formal thoracotomy was rapidly done by resecting a five inch segment of the third costal cartilage and rib. Blood was seen to be flowing from an opening, one half inch in diameter, in the upper lateral wall of the pericardium. This opening was enlarged and a one half to three quarter inch laceration was visible at the junction of the superior vena cava and right auricle anteriorly. For more adequate exposure the thoracotomy was extended medially resecting completely a section of the sternum over this area. The laceration was now seen to be about one half in the superior vena cava and one half in the auricle. This wound was closed with a double layer of fine silk sutures. The pericardium was closed tightly after further exploration showed no other myocardial or pericardial damage.

The laceration of the upper lobe of the right lung was closed using a double row of intestinal catgut. The pleural cavity was irrigated with 1,500 cc of normal saline solution. Further exploration of lung and diaphragm showed no damage. How the bullet got to the lower abdominal area was undecided. Thoracotomy openings were closed airtight. The lung was expanded under positive pressure. A laparotomy was then performed and disclosed no intraperitoneal or retroperitoneal hemorrhage, and no diaphragmatic or viscous damage. The mystery was unsolved as to how the bullet had descended into the pelvis.

For one hour after the first severe hemorrhage at the outset of surgery the anesthetist was not able to detect the blood pressure. All anesthesia was stopped during this period, only oxygen being administered. At this time the patient appeared almost dead. Each labored respiration appeared to be his last. Following the operation, bronchoscopic aspiration and complete intercostal nerve block were done on right side.



Fig 1

Fig 1—Right hemopneumothorax with mediastinal shift to the left



Fig 2

Fig 2—Position of machine-gun bullet on anteroposterior view of pelvis



Fig 3

Fig 3—Position of machine-gun bullet on lateral view of lumbar vertebrae



Fig 4

Fig 4—Venogram anteroposterior view indicating position of bullet to be in left common iliac vein

The total duration of surgery was two and one half hours. During this period the patient received 2,500 c.c. of blood by two routes (arm and leg) simultaneously, under positive pressure a large part of the time. He received 500 c.c. of blood preoperatively and an additional 500 c.c. on the postoperative ward making a total of 3,500 c.c. of blood in about five hours' time.

**Postoperative Course.**—Following operation the patient was very apprehensive for the first six or seven days, with a rapid pulse and respiration. Blood pressure never fell below 100 systolic and pulse pressure was always 40 or above. He received continuous nasal oxygen during this period, and daily venous pressure readings were made. Decompression with Wangensteen suction was used for first three days postoperatively. During the decompression period, 5 per cent glucose in saline solution was given to insure adequate urinary output and chloride balance.



Fig 5

Fig 5.—The patient three days after removal of missile (April 9, 1945).



Fig 6

Fig 6.—X-ray view seventeen days after admission to field hospital (April 9, 1945). Lungs have practically cleared.

The pericardial sac was aspirated on the second and third postoperative days with the following results:

March 24, 1945, 225 c.c. of sanguineous fluid were obtained. March 25, 1945, 65 c.c. of serosanguineous fluid were obtained. The highest venous pressure reading was 18.5 cm. of water. After the third postoperative day venous pressure was never above 14.5 cm. of water. Chest aspirations were performed according to radiographic findings. Frequent hematocrit readings were made and blood was given as indicated. Altogether the patient received 3,500 c.c. of blood during the postoperative course at the field hospital.

Penicillin was administered intramuscularly (25,000 U) every three hours for twelve days following operation. A similar amount was given for six days following the last operation for removal of the foreign body. Vitamin therapy was administered from the beginning.

April 5, 1945, a venogram done by injecting diodrast in the left femoral vein indicated a machine gun bullet in the left common iliac vein just below the bifurcation of the inferior vena cava (Fig. 4). Attempts to take a lateral venogram were unsuccessful.

April 6, 1945, under gas oxygen, ether anesthesia, a retroperitoneal exploration for the foreign body was performed. An elliptical incision was made just above and medial

to the left iliac crest. The left common iliac vein was exposed and tape was placed proximally and distally to the location of the missile. The occlusion of the vein wall above was done in the endeavor not to allow any clot to escape toward the heart. The vein was incised and a rather large amount of fibrinous exudate and blood clot attached to the bullet and vein wall was exposed and subsequently removed. The left common iliac vein was then ligated above and below the site of injury.

On the third day following the removal of the missile the patient was alert and his general condition was very satisfactory (Fig. 5). On the same day an x-ray view of the chest showed an enlarged cardiac shadow to the left. Lung fields were practically clear (Fig. 6).

Heparin was administered (one ampule a day for four days).

For the first three or four days following operation there was some pain and moderate swelling of the left thigh and leg which gradually subsided during the following seven days.

All incisions healed primarily except the anterior thoracotomy incision where the third rib was resected. This incision became secondarily infected and there was still slight seropurulent drainage when the patient was evacuated from the 33rd Field Hospital.

Personal communications from the patient during the postoperative course in base hospitals in Italy and at Walter Reed Hospital in Washington, D. C., indicated that his progress was satisfactory.

The following personal information was forwarded on Aug. 9, 1945, from Colonel R. A. Griswold, Chief of Surgical Service, Walter Reed General Hospital, Washington, D. C.:

"Your patient is at present here and was operated upon by me last week. When he got here he was in excellent condition with all wounds well healed, but had a large shadow on the left side of the heart with compression of the left ventricle as seen on diodrast angiocardiogram. Pictures with diodrast in the left ventricle showed that it was indented and compressed by this extracardiac mass which we thought was probably an encapsulated hemioma in the pericardium since there was no fever, increased white count, or other signs of sepsis.

"I removed the left fifth costal cartilage and found that the mass was a thick walled, localized collection of pus in the pericardium. About 200 c.c. of pus was removed along with a piece of wool fabric about 3 cm. in diameter which was the cause of the abscess. Cultures were sterile. The location of the abscess was so far posterior that it had to be approached transpleurally. I unroofed it by removing a portion of the lateral abscess wall about 4 cm. in diameter so that it could drain adequately into the pleura. He is getting along well and should be out of the hospital within a few weeks."

Further communication from the patient revealed that he had an osteoperiosteal graft on March 8, 1946, at the Fitzsimmons General Hospital in Denver, Colo., to repair an anterior herniation of the chest wall, thus providing better heart protection. This operation was very satisfactory.

# Editorial

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## The Society for Vascular Surgery

WITH an appreciation of the importance of vascular diseases of all types, and with a consequently increasing interest in such diseases, the establishment of The Society for Vascular Surgery attracts attention. During World War II the importance of peripheral vascular injury was particularly emphasized. As a result of exposure to cold, either on the damp ground, in the water, or in the air, changes in the peripheral vessels were frequent, some of only a temporary nature, whereas, others were so extensive that viability of the area supplied by the injured vessels could not be maintained. The need for additional investigation in such instances became evident. Although both traumatic and crymotic vascular injuries observed during the war were dramatic and attracted considerable attention and were responsible for calling attention to the importance of lesions of the vascular system, it must be emphasized that congenital and spontaneously occurring diseases of the vessels as well as traumatic lesions are of great importance during peace time. These conditions not only produce suffering and disability but also are likely to shorten materially the life span of the afflicted individual. Nothing could be more catastrophic or tragic than the sudden death from pulmonary embolism in a patient apparently normally convalescing from a simple operative procedure.

Advances in vascular disease can be made in a number of ways: clinical investigation of patients, noting the response of various therapeutic measures in the normal individuals and in those with vascular lesions. In many instances combined investigations by physiologists, pharmacologists, internists, and surgeons are necessary in order to understand the underlying pathology in vascular lesions and to evaluate the therapy. Also, much can be accomplished in the study of diseases of the vascular system as well as in other diseases by animal experimentation. It is becoming increasingly more apparent that in large hospitals vascular services should be established in order to permit these combined studies. In this way the patient with vascular disease, whether spontaneously occurring or whether the result of trauma or other causes, will receive better care.

Dr. Geza de Takats, who is recorder for the new society, has summarized the objectives of the society as follows: (1) to promote research and study in vascular disease; (2) to define more clearly the role of surgery in this field; (3) to promote and encourage adequate teaching of vascular diseases to students, interns, and residents; (4) to encourage hospitals to develop special sections in vascular surgery and to provide special training in vascular surgery for young surgeons interested in this field; (5) to pool the experiences and knowledge of

to the left iliac crest. The left common iliac vein was exposed and tape was placed proximally and distally to the location of the missile. The occlusion of the vein wall above was done in the endeavor not to allow any clot to escape toward the heart. The vein was incised and a rather large amount of fibrous exudate and blood clot attached to the bullet and vein wall was exposed and subsequently removed. The left common iliac vein was then ligated above and below the site of injury.

On the third day following the removal of the missile the patient was alert and his general condition was very satisfactory (Fig 5). On the same day an x-ray view of the chest showed an enlarged cardiac shadow to the left. Lung fields were practically clear (Fig 6).

Heparin was administered one ampule a day for four days.

For the first three or four days following operation there was some pain and moderate swelling of the left thigh and leg which gradually subsided during the following seven days.

All incisions healed primarily except the anterior thoracotomy incision where the third rib was resected. This incision became secondarily infected and there was still slight seropurulent drainings when the patient was evacuated from the Third Field Hospital.

Personal communications from the patient during the postoperative course in base hospitals in Italy and at Walter Reed Hospital in Washington, D. C., indicated that his progress was satisfactory.

The following personal information was forwarded on Aug 9, 1945, from Colonel R. A. Griswall, Chief of Surgical Service, Walter Reed General Hospital, Washington, D. C.:

"Your patient is at present here and was operated upon by me last week. When he got here he was in excellent condition with all wounds well healed, but had a large shadow on the left side of the heart with compression of the left ventricle as seen on diolast angiocardigrams. Pictures with diolast in the left ventricle showed that it was indented and compressed by this extracardiac mass which we thought was probably an encapsulated hematoma in the pericardium since there was no fever, increased white count, or other signs of sepsis.

"I removed the left fifth costal cartilage and found that the mass was a thick walled, localized collection of pus in the pericardium. About 200 cc of pus was removed along with a piece of wool fabric about 1 cm in diameter which was the cause of the abscess. Cultures were sterile. The location of the abscess was so far posterior that it had to be approached transpleurally. I unroofed it by removing a portion of the lateral abscess wall about 4 cm in diameter so that it could drain adequately into the pleura. He is getting along well and should be out of the hospital within a few weeks."

Further communication from the patient revealed that he had an osteoperiosteal graft on March 8, 1946, at the Fitzsimmons General Hospital in Denver, Colo., to repair an anterior herniation of the chest wall, thus providing better heart protection. This operation was very satisfactory.

## Book Reviews

**Peripheral Vascular Diseases.** By Edgar V. Allen, B.S., M.A., M.D., M.S., F.A.C.P., Division of Medicine, Mayo Clinic; Nelson W. Barker, B.A., M.D., M.S., F.A.C.P., Division of Medicine, Mayo Clinic; Edgar A. Hines, Jr., M.D., B.S., M.A., M.S., F.A.C.P., Division of Medicine, Mayo Clinic; and associates in the Mayo Clinic. Pp 871, with 386 illustrations. Philadelphia, 1946, W B Saunders Company \$10

This is a comprehensive treatise and in the reviewer's opinion the best of the several books on the same subject which have been published during the past few years. The three principal authors are recognized authorities in their field and have a combined experience to draw from which is unsurpassed anywhere. Eleven other contributors have written portions of the book which deal with specialized phases of the subject and give a uniform excellence to the whole book.

Each disease is considered as an entity. The student will find much pertinent knowledge concerning the history and methods of investigation of each subject. The practitioner will find adequate sections on diagnosis and treatment. The teacher will find it an excellent reference book. The bibliography is well chosen and adequate.

The work is dedicated to the late George E. Brown of the Mayo Clinic. In the reviewer's opinion the hope of the authors has been fulfilled. It is a worthy monument.

**Harvey Cushing, a Biography.** By John F. Fulton. Pp 754, with 89 illustrations. Springfield, Ill, 1946. Charles C Thomas, Publisher.

In his will, Cushing made provision for the publication of his biography should it be deemed "of interest and help to medical students." Fulton has more than met these conditions, and has edited and integrated a vast body of source material which he has bound together with an easy flowing narrative. Written and composed in the manner of Cushing's "Osler," to which it is a worthy companion piece, the author has selected liberally, but critically, from Cushing's prolific and illuminating diaries, correspondence, and publications.

With just enough family, geographic, and genealogic background, the biography passes quickly through his youth, pauses a little longer in the "bright college years" at Yale, and settles down to a sustained pace with his entrance into Harvard Medical School and early years at the Massachusetts General Hospital. The picture emerges of Cushing, a restless spirit "hot to the touch," consecrated to medicine, fired by a tremendous ambition, and sustained by boundless energy. Through the medium of his diary and family correspondence is presented an account of medicine and surgery in Boston in the days of the amphitheatre and private home, of surgical Titans and the hazards of anesthesia.

Then follow, in sharp contrast, his life as surgical resident at the Johns Hopkins, but newly sprung from the brow of Aesculapius, the interesting development of his relations with Halsted, his sustained friendship with Welch, and the beginnings of all important relations with Sir William Osler, who led him "on the severe ascent of high Parnassus." Following his year of study abroad with Kocher, Kronecker, and Sherrington and the widening of his outlook to an international horizon, so important to his later development, there is the return to Baltimore—the "lateh kayer" days—the ripening of his surgical thinking, contributions to surgical technique and its teaching, and the gradual development of the relatively unexplored field of neurologic surgery. This part of the book, closing with a record of his negotiations with Harvard which led to the Moseley Professorship and the Brigham Hospital, is particularly well done, and shows the breadth of Cushing's surgical foundation.



After a most interesting account of settling in Boston and at Harvard, there follows the narrative of the war years, taken largely from his Homeric diary which serves to project Cushing against the background of the war. In the years that follow, we find H. C. back at Harvard. There are years of intense and tremendously varied activity, years of promise fulfilled, punctuated by a steady stream of honors in this country and abroad. By choice, references to the more technical phases of these clinical years have been deliberately curtailed in favor of historical and personal material.

The closing chapters deal with Cushing's return to Yale, a period rich in literary accomplishment, but tempered somewhat by ill health and forced inactivity. Much time was spent in the arrangement and disposition of his books, in writing, and in the preparation of the bibliography of Vesolius, a work which he did not quite have time to finish. In 1939, his 70th birthday was celebrated with a tremendous expression of affection and esteem, and shortly thereafter he received the unique honor of election to the Royal College of Physicians. Later that year, in the Fall, he succumbed to a coronary occlusion.

The book cannot fail to inspire and stimulate medical students, but even more than that, it is the record of a great figure and personality during the coming of age of surgery in America. Well illustrated and profusely documented, it is easily written and objective to a high degree, although the inclusion of many of Cushing's facile sketches and the numerous quotations give the book almost the character of an autobiography. As Cushing was a man of such broad interests and attainments, the volume should have a wide general appeal, as a personal record of his contemporaries, and as a commentary on his times, it should prove of lasting interest and real significance.

**Operative Gynecology.** By Richard W. Telande, M.D., Professor of Gynecology, Johns Hopkins University, Baltimore, Md. Pp 725, with 313 illustrations. Philadelphia, 1946, J. B. Lippincott Company.

Telande, who heads the department of gynecology at Johns Hopkins Hospital and Medical School, has prepared this book for use particularly by graduate students during specialty training and as a reference book for clinical work for general surgeons. It is also of interest to the specialist. It is not a reference book but presents in detail the methods in use in his own department and the reasons for their adoption. It is, then, a most practical presentation and will receive wide acceptance for this reason.

Detailed consideration is given to pre and postoperative study and care. In particular, the Hopkins routines for the handling of the bladder after pelvic surgery are discussed at length and the results are reported to be really excellent.

The indications and contraindications of most of the useful gynecologic surgical procedures are presented clearly and soundly. Surgical techniques are given in detail and clearly. One is surprised at the absence of descriptions of techniques for local anesthesia and of the Wertheim operation. The two paragraphs dealing with the details of the x-ray therapy of cervical carcinoma are in need of revision.

The illustrations are magnificent and in most generous number. They have been produced by a number of artists. They might well serve as standards of excellence toward which others might strive.

This is undoubtedly the best book in its field and is to be recommended for wide use.

# SURGERY

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## Original Communications

### CHEMOSURGICAL TREATMENT OF CANCER OF THE EAR: A MICROSCOPICALLY CONTROLLED METHOD OF EXCISION

FREDERIC D. MOHS, M.D., MADISON, WIS.

*(From the Department of Surgery and the Mc Millen Memorial Laboratory,  
University of Wisconsin Medical School)*

**T**HE development of the chemosurgical method for the microscopically controlled excision of cancer has previously been described.<sup>1,2</sup> The use and evaluation of the method in the treatment of cancer in specific sites, such as the lip<sup>3</sup> and the nose,<sup>4</sup> has been reported. The present article deals with the chemosurgical treatment of cancer of the ear and includes the analysis of the therapeutic results in a consecutive series of 107 lesions treated over the period of nine and one-quarter years ending Sept. 29, 1945, which date is nine months prior to this writing. Inasmuch as the behavior of squamous-cell carcinoma is much different from that of basal-cell carcinoma, the two histologic types are considered separately except in regard to the chemosurgical technique which is the same for both types.

#### TECHNIQUE

The chemosurgical technique by which cancer of the ear may be excised under systematic microscope control will be described in the case report which follows.

**CASE REPORT.**—The lesion pictured in Fig. 1 was first noticed six months previous to the patient's first visit to the Chemosurgery Clinic. It began as a nodule which was covered with skin at first but which became ulcerated after a few weeks. He was referred to a radiologist who in turn referred the patient for chemosurgical treatment because he believed that the cartilage might be damaged by radiation therapy.

The lesion was a firm nodule 11 mm in diameter. It was elevated 3 mm. above the level of the concha of the ear. There was a central ulcer, in the base of which protruded papillae with slightly hyperkeratotic tips. The lesion was adherent to the underlying cartilage. No enlargement of the regional lymph nodes was palpated.

The first step in treatment was the application of dichloroacetic acid to the part of the lesion covered by skin. This keratolytic chemical served to render the skin permeable

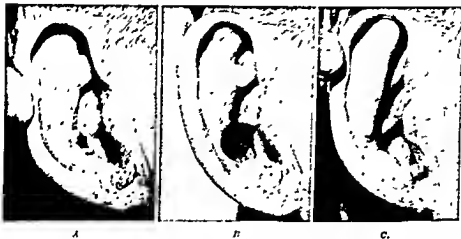
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to the fixative which was next applied. The fixative consists of a paste made up according to the following formula: 40 Gm. of silicone (4 mesh mesh), 11 Gm. of powdered sugar, and 250 cc. of a saturated solution of zinc chloride. This material was applied in a thickness of about 6.5 mm. layer.

The treated area was covered by a layer of cotton and then by an antiseptic layer of cotton on which petrolatum was spread to form a nonadherent dressing. The dressing was made fast by means of adhesive tape. The patient was instructed to take 150 Gm. of acetylsalicylic acid as required to control the pain. He was treated as an out-patient.

On the second day a layer of tissue about 3 mm. thick was excised with a scalpel. There was no pain or bleeding produced by the operation because the incision was made through killed and fixed tissue. That cancer was present at this level was evident to gross inspection, so the fixative paste was immediately reapplied in a depth of about 6.5 mm. later. A frozen section of the fixed tissue contained squamous-cell carcinoma of grade 2 malignancy.



A

B

C

Fig. 1—A, Squamous-cell carcinoma grade 2 malignancy, of Group B (average diameter 1 to 2 cm.), located in the concha. B, Granulation tissue after separation of the final layer of fixed tissue, including a layer of cartilage, and after healing was under way. C, Healed lesion, two months later. Patient is free of cancer after three and one-half years.

On the third day the cancer tissue was still grossly visible and was seen to involve the perichondrium under the central part of the neoplasm. There was, however, no visible erosion of the cartilage itself. Accordingly, the fixative paste was not applied to the cartilage but only to the tissues at the periphery.

On the fourth day a layer of tissue 1 mm. in thickness was excised from the periphery. When no cancer could be detected by gross examination the excised layer was divided into five specimens of convenient size, and their locations were mapped on the lesion (using mercuricchrome) and on a pad of paper (Fig. 2, A).

Frozen sections were made by cutting through the undersurface of each of the five specimens and by staining with hematoxylin and eosin. Each section was scanned under the microscope and the areas of remaining cancer located on the map as indicated by the two stippled areas in Fig. 2, A.

Further application of the fixative was limited to the two cancerous areas. On the next day the specimens from these areas were found to be free of cancer (Fig. 2, B). The lesion was covered with a petrolatum gauze dressing.

One week later the remaining thin layer of fixed tissue had become separated from the living tissues and could be removed by snipping the holding strands of fibrous tissue with sharp-pointed scissors. The necrotic portions of cartilage were also removed. (In

this series the average time at which the basal layer could be removed was 7.4 days with a range of from 4 to 12 days.) The granulations (Fig. 1, B) were kept covered with petrolatum gauze until the wound had healed two weeks later. The final scar and defect were barely noticeable (Fig. 1, C).

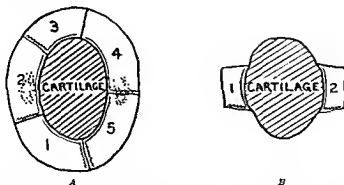


Fig. 2.—Maps showing locations of specimens removed on two successive days from the lesion shown in Fig. 1. A, stippled areas represent two areas of cancer. On the following day specimens from these two areas were free of cancer (B).

As in this case, many cancers of the ear extend onto the underlying cartilage. When this occurs it is necessary to section only the tissues at the periphery. If, however, the cancer has eroded through the cartilage, the defect is grossly visible upon exposure of the cartilage and microscopic study of the tissues beyond the invaded cartilage is indicated.

When invasion of the entire thickness of the ear has occurred it is necessary to remove the full thickness of the ear in the involved region (Fig. 3). Cancers which extend far beyond the ear proper are not infrequently encountered (Fig. 4). Some were followed out for many centimeters beyond the region in which the cancer was originally thought to be confined.

The extension of cancer onto the bone necessitates the destruction of a thin layer of bone to assure complete removal of the neoplasm. Cancerous erosion of the bone produces a honeycombed area which is grossly visible; this involved bone may be fixed with the zinc chloride fixative and removed layer by layer with chisels or rongeurs, until solid, cancer-free bone is reached.

Removal of large lesions involving the helix of the ear may necessarily result in the formation of a niche in the normal contour of the ear. Such defects are relatively easy to repair, however, because a maximum amount of normal structure is preserved as a base for plastic reconstruction.

In cases in which the entire ear was removed there was never any stenosis of the canal (Fig. 5). However, following the removal of advanced lesions involving the concha and the entire circumference of the canal, there may be some tendency for stenosis to occur (Fig. 6). Therefore, it is advisable to keep the canal distended during and immediately after healing. For this purpose petrolatum gauze wicks or catheter tips may be used.

Cancers involving the canal and extending into the middle ear and around the mastoid and styloid processes have been followed out by the chemosurgical

technique, using long, slender scalpels and forceps. Unfortunately, however, the lesions of this type encountered in this series all have been so advanced that the patients succumbed either to carcinomatous invasion of deeper structures or to metastasis.

Difficulty due to hemorrhage is not encountered during the chemosurgical treatment of carcinomas of the ear, with the exception of those extending into the region of the superficial temporal or external carotid arteries. If, during the excision of the layers of fixed tissue, there is bleeding, it usually can be controlled by the application, under pressure, of a small piece of gauze impregnated with the zinc chloride fixative. If bleeding should occur during separation of the final layer of fixed tissue, a suture-ligature may be required.

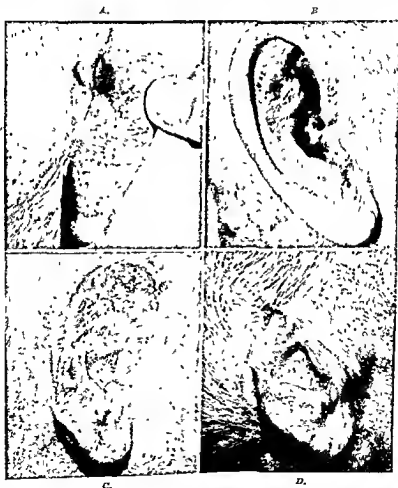


FIG. 3.—A, Squamous-cell carcinoma, grade 2 malignancy, of Group D (average diameter, 3 cm. or more). The lesion began in the concha but extended through the full thickness of the ear (B). C, Granulation tissue thirteen days after the start of treatment. D, Healed lesion after two months. There was no cancer present when the patient died of other disease after two and one-quarter years.

## THERAPEUTIC RESULTS IN CASES OF SQUAMOUS-CELL CARCINOMA OF THE EAR

A total of fifty-two patients with squamous-cell carcinomas of the ear was chemosurgically treated. The extent of the lesions ranged from very early to extremely advanced. Thirty per cent of the cancers were recurrent following previous surgical or radiation treatment.

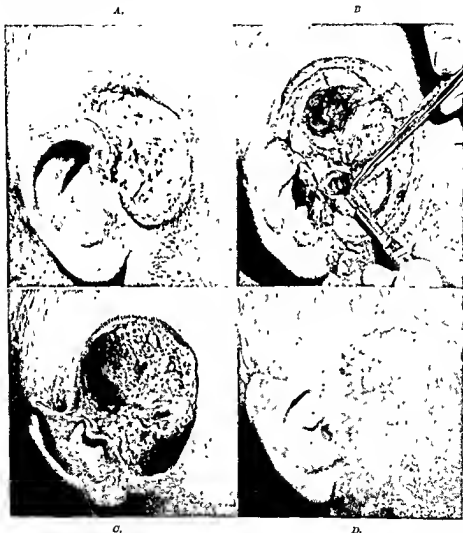


Fig. 4—A, Squamous-cell carcinoma grade 3 malignancy, of Group D (average diameter, 3 cm. or more). The lesion began in the preauricular region, and despite repeated roentgen ray and radium treatments over a period of one and one-half years, it extended back into the pinna but more extensively into the scalp and cheek. B, Lesion under treatment after one week, showing white, fixed tissue with markings used to orient specimens removed for microscopic study. The two black areas contained cancer and were still under treatment. The lower area is shown in process of excision. A cancer-free plane was reached on the eighth day. The layer of fixed tissue, 1 to 2 mm. thick which at this stage was adherent was removed seven days later. C, Granulation tissue on the seventeenth day showing exposed zygoma. D, Healed lesion. The patient remains free of cancer after six years.

**Primary Lesion.**—Of the fifty-two patients in this series, fifty were followed for six months or more. In this group of fifty patients, the primary squamous-cell carcinoma was eradicated in forty-six (92 per cent).

The four cancers which were not eradicated were far advanced. One was a massive carcinoma with a malignancy of grade 3, it eroded through the temporal bone into the transverse venous sinus. The second was a deep seated cancer with a malignancy of grade 3, involving the ear canal along with the temporomandibular joint and surrounding structures. The third was a massive carcinoma with a malignancy of grade 2, which arose in the canal. There was also cervical metastasis, therefore no drastic effort was made to remove a recurrent mass which extended into the middle ear. The fourth lesion not eradicated was a carcinoma which arose in the region of the middle ear. It extended outwardly in the ear canal and inwardly around the great vessels into the oropharynx.



Fig. 5.—A, Squamous cell carcinoma, grade 4 malignancy, of Group D. The lesion began on the antihelix and in eighteen months destroyed the ear. B, Granulation tissue four weeks after start of treatment showing mastoid process, which was exposed because of cancerous invasion of the periosteum. The necrotic layer of bone sloughed off one month later. C, Healed lesion showing patent canal. The patient was kept under observation by his family doctor, and no evidence of cancer was found for nearly two years when metastasis in a deep cervical node was stated to have suddenly made its appearance. When he returned to the hospital the node was too large to justify radical dissection in consideration of the patient's advanced age.

In general, it may be stated that any carcinoma of the external ear may be removed by the chemosurgical method if there is not actual involvement of underlying vital structures, such as the brain with its venous sinuses, the carotid, or jugular vessels.

**End Results After Six Months or More**—While end results after six months are of limited value for the comparison of the results with those obtained by other methods, they form a fairly accurate expression of the ultimate outcome. This is so because residual cancer, if present after chemosurgical treatment,

usually makes itself evident well within the six-month period because it is not deeply buried in a surgical incision, nor is it kept in abeyance by an atrophic radiation scar. Moreover, metastases usually become evident before a period of six months has passed

The fifty-two cases of squamous cell carcinoma were divided into "indeterminate" and "determinate" groups following the example of Martin, MacComb, and Blady.<sup>2</sup> The indeterminate group includes: (1) the cases of patients who died of intercurrent disease without evidence of recurrence and (2) those who were lost from observation without recurrence. The determinate group is composed of: (1) the cases of patients in whom unsuccessful results were obtained (the patients who have died of cancer, who have been lost from observation with cancer, or who are living with cancer) and (2) the cases of patients in whom successful results were obtained (the patients who remained free of cancer for six months or more)



A.

B.

C.

Fig 6—A, Basal-cell carcinoma, invasive histologic type, of Group D (average diameter, 3 cm or more). The lesion began fourteen years previously on the tragus. It continued to spread back into the canal and into the ear lobe despite repeated treatments with radium, roentgen ray and electrosurgical procedures. B, Granulation tissue sixteen days after the start of chemosurgical treatment. That the cancer had extended considerably more widely than would have been supposed from clinical examination is indicated by the size of the defect. The white area anterior to the canal is the articular process of the mandible. The branch of the facial nerve supplying the frontalis muscle was interrupted. Five months later an island of cancer, which apparently had been cut off from the main mass by some previous treatment, was discovered in the infra-auricular region. After two years no more cancer has appeared, but the diameter of the canal has been reduced to 1 millimeter (C).

In the fifty cases of squamous-cell carcinoma in the determinate group, the rate of cure after six months or more was 80 per cent (Table I).

*Three-Year and Five-Year End Results.*—An intensive follow-up program had as its goal the observation of every patient for at least five years. In this series only one patient was lost from observation.

In the three-year period successful results were obtained in 74.2 per cent of the thirty-one cases in the determinate group (Table I).

In the five-year period successful results were obtained in 64.3 per cent of the fourteen cases in the determinate group (Table I).

*Effect of Size of Lesion on Prognosis.*—The fifty lesions included in the determinate group in the six-month period were divided into four groups accord-



TABLE I. END RESULTS FOR SQUAMOUS CELL CARCINOMA OF THE EAR AFTER PERIODS OF SIX MONTHS, THREE YEARS, AND FIVE YEARS

	SIX MONTH PERIOD	THREE YEAR PERIOD	FIVE YEAR PERIOD
Total number of cases	52	35	19
Indeterminate group			
Patients dead from other causes with out recurrence	1	4	5
Patients lost from observation with out recurrence	1	0	0
Total number	2	4	5
Determinate group			
Total number	50	31	14
Unsuccessful results			
Patients dead from cancer present at time of death	10	8	5
Patients lost from observation with cancer	0	0	0
Patients living with cancer	0	0	0
Total number	10	8	5
Successful results			
Patients free from cancer for six months or more	40		
Patients free from cancer for three years or more		23	
Patients free from cancer for five years or more			9
Six month end results			
Total number of cases with successful results divided by total number of determinate cases (40 - 50)	80.0%		
Three-year end results			
Total number of cases with successful results divided by total number of determinate cases (23 - 31)		74.2%	
Five year end results			
Total number of cases with successful results divided by total number of determinate cases (9 - 14)			64.3%

This series includes the cases of all patients with histologically proved squamous-cell carcinomas, both early and advanced, previously untreated and recurrent, admitted to the Chemosurgery Clinic from Aug. 29, 1936, to Sept. 29, 1945 for the six-month group from Aug. 29, 1936 to Jan. 10, 1943, for the three-year group, and from Aug. 29, 1936 to Feb. 14, 1941, for the five-year group.

ing to their average diameter. Group A, under 1 cm.; Group B, 1 to 2 cm (Fig. 1); Group C, 2 to 3 cm.; and Group D, 3 cm. or more (Figs. 3 to 5). The measurements always refer to the size as clinically determined before treatment was begun rather than to the size as determined during the course of chemosurgical treatment.

As was to be expected, the rate of cure in Group A was high (100 per cent) but tapered off in the larger size groups (Table II).

*Effect of Previous Treatment on Prognosis*.—Thirty per cent of the fifty patients with squamous-cell carcinomas in the determinate group had received previous unsuccessful treatment by means of some surgical or radiation procedure either alone or in combination. Although it was possible to salvage

TABLE II. EFFECT OF SIZE OF SQUAMOUS CELL CARCINOMA ON PROGNOSIS

GROUP	ULCER DIAMETER (CM.)	NUMBER OF LESIONS	SUCCESSFUL RESULTS	
			NUMBER	PER CENT
A	Under 1	16	16	100.0
B	1 to 2	15	13	86.7
C	2 to 3	6	3	50.0
D	3 or more	13	8	61.5
All groups		50	40	80.0

53.3 per cent of the patients with recurrent lesions, the rate of cure was well below the 91.4 per cent attained in the group of patients who gave no history of previous treatment (Table III). The poorer prognosis in patients with recurrent lesions was due largely to the delay and the increase in extensiveness which occurred during the period of inadequate treatment.

TABLE III. EFFECT OF PREVIOUS TREATMENT OF SQUAMOUS CELL CARCINOMA ON PROGNOSIS

	NUMBER OF PATIENTS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
Previously treated	15	8	53.3
Previously untreated	35	32	91.4

*Effect of Histologic Grade of Malignancy on Prognosis*—The fifty squamous-cell carcinomas, upon classification on the basis of Broders' four grades of malignancy, were distributed as follows: grade 1, 24 per cent; grade 2, 48 per cent; grade 3, 20 per cent, and grade 4, 8 per cent.

In agreement with Broders' conclusions,<sup>6</sup> the prognosis in the present series was strongly affected by the grade of malignancy as indicated by the fact that the rate of cure was 91.7 per cent for lesions with a malignancy of grades 1 and 2 but dropped to 60 and 25 per cent for lesions with a malignancy of grades 3 and 4, respectively (Table IV). The reason for this drop in rate of cure was due largely to the greater tendency toward metastasis exhibited by cancers of higher malignancy.

TABLE IV. EFFECT OF HISTOLOGIC GRADE OF MALIGNANCY OF SQUAMOUS CELL CARCINOMA ON PROGNOSIS

GRADE	NUMBER OF LESIONS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
1	12	11	91.7
2	24	22	91.7
3	10	6	60.0
4	4	1	25.0

*Effect of Metastasis on Prognosis*—The prognosis in cases of carcinoma of the ear is much worse in those in which cervical metastasis has occurred. Thus, in the fifty patients in the determinate group there were seven who eventually developed cervical metastases, and all of these patients died from cancer. In contrast, in the group of forty-three patients who did not develop metastases there was a rate of cure of 93 per cent (Table V).

The metastases were diagnosed at the beginning of treatment in three cases, while in four others they were found at checkup examinations. There

TABLE V. EFFECT OF METASTASIS ON PROGNOSIS

	NUMBER OF PATIENTS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
With metastasis	7	0	0
Without metastasis	43	40	93

were four patients who at the onset of treatment had enlarged regional nodes which later returned to normal upon removal of the infected primary lesion.

No prophylactic neck dissections were done in this series, but a policy of close postoperative observation was followed. Unfortunately, the four patients who developed nodes after removal of the primary lesion failed to return as soon as requested, therefore, the metastases became extensive. In all of the patients who developed metastases there had been large primary cancers of higher than usual malignancy (two each were classified as grades 2 and 3 and three were classified as grade 4). In view of these circumstances it probably would be wise to consider prophylactic dissection of the cervical nodes for patients having large, highly malignant, primary cancers. This would seem to be indicated particularly in patients who cannot be relied upon to return regularly for checkup examinations.

In three patients of this series surgical and chemosurgical dissection of metastatic cervical nodes was carried out, while in six patients palliative roentgen therapy was given either alone or in conjunction with the aforementioned surgical procedures. These procedures were of definite temporary benefit and they made it possible to delay the fatal termination for as long as three years.

*Effect of Site of Origin on Prognosis*—The fifty squamous-cell carcinomas in patients in the determinate group arose in the seven regions which are listed in Table VI. A majority (twenty-eight) of the lesions were located on the outer rim of the ear and on the anterior surface, and in these locations the prognosis was uniformly good, the rates of cure were as follows: helix and lobe, 100 per cent, antihelix and crura, 93.8 per cent, and concha, 100 per cent.

The rates of cure were somewhat lower for cancers arising on the posterior surface of the ear (66.7 per cent), in the postauricular region (75 per cent), and in the preauricular and tragal regions (75 per cent). The lowest rate of cure was for lesions arising in the canal and deeper structures; none of the four

TABLE VI. EFFECT OF SITE OF ORIGIN OF SQUAMOUS CELL CARCINOMA ON PROGNOSIS

SITE	NUMBER OF LESIONS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
Helix and lobe	10	10	100.0
Antihelix and crura	16	15	93.8
Concha	2	2	100.0
Canal and deeper structures	4	0	0.0
Posterior surface	6	4	66.7
Postauricular region	8	6	75.0
Preauricular and tragal region	4	3	75.0
All sites	50	40	80.0

in this group were cured. In general, the more medial the site of origin the worse was the prognosis. Conversely, the nearer to the outer rim of the ear the better the prognosis tended to be. This tendency was in part due to the fact that the lesions arising more medially would more quickly erode into underlying vital structures and in part due to the richer lymphatic supply in the deeper structures with the consequent greater tendency toward metastatic spread. Most of the lesions which metastasized arose on the posterior surface of the ear or in the adjacent postauricular region; these usually soon invaded the posterior-auricular groove, and in this location any movement of the ear strongly traumatized the cancer. This trauma doubtless increased the tendency for metastasis to occur.

The poor results with the four lesions arising in the canal or deeper structures were ascribed to the fact that in three metastasis had occurred, while in the fourth the carcinoma, which arose in the region of the middle ear, had spread medially to the oropharynx. There is no reason why less advanced lesions of the canal should not respond well to chemosurgical treatment.

#### THERAPEUTIC RESULTS IN CASES OF BASAL-CELL CARCINOMA OF THE EAR

A consecutive series of fifty-five patients with basal-cell carcinomas of the ear was treated chemosurgically. In this group, 25.5 per cent of the cancers were recurrent following previous surgical or radiation treatment. There was no instance of metastasis.

*End Results After Six Months or More*—Of the fifty-five patients with basal-cell carcinoma followed for six months or more, fifty-one were in the determinate group. Of this group, forty-seven were successfully treated, so the rate of cure was 92.2 per cent (Table VII).

Treatment was unsuccessful in four patients. Two of these had extensive involvement of the temporal bone, so that complete removal was not feasible. Two others had lesions arising deep in the canal and they could not be removed completely because of extensive involvement in the vicinity of the middle ear and deeper structures.

*Three-Year and Five-Year End Results.*—In the series of thirty-five patients followed for three years or more, there were thirty-one in the determinate group. In the latter group there were twenty-seven successfully treated patients; therefore, the rate of cure after three years or more was 87.1 per cent (Table VII).

There were twenty-five patients followed for five years or more and of these twenty-one were in the determinate group. Of those in the latter group, seventeen were successfully treated, so the rate of cure after five years or more was 81 per cent (Table VII).

It will be noted that there were four failures in the six-month group, four in the three-year group, and four in the five-year group. This circumstance was due to the fact that all of the failures occurred early in the course of the project. Since the total number of cases in the groups followed for the longer terms was smaller, there is in them a consequent lower rate of cure. In the group of thirty-eight patients with basal-cell carcinoma of the ear treated during the past eight years, there have been no failures.

TABLE VII. END RESULTS FOR BASAL CELL CARCINOMA OF THE EAR AFTER PERIODS OF SIX MONTHS, THREE YEARS, AND FIVE YEARS

	SIX MONTH PERIOD	THREE-YEAR PERIOD	FIVE YEAR PERIOD
Total number of cases	55	35	25
Indeterminate group			
Patients dead from other causes with out recurrence	3	3	3
Patients lost from observation with out recurrence	1	1	1
Total number	4	4	4
Determinate group			
Total number	51	31	21
Unsuccessful results			
Patients dead from cancer present at time of death	3	3	3
Patients lost from observation with cancer	1	1	1
Patients living with cancer	0	0	0
Total number	4	4	4
Successful results			
Patients free from cancer for six months or more	47		
Patients free from cancer for three years or more		27	
Patients free from cancer for five years or more			17
Six month end results			
Total number of cases with successful results divided by total number of determinate cases (47 + 51)	92.2%		
Three year end results			
Total number of cases with successful results divided by total number of determinate cases (27 + 31)		87.1%	
Five year end results			
Total number of cases with successful results divided by total number of determinate cases (17 + 21)			81.0%

This series includes the cases of all patients with histologically proved basal-cell carcinoma, both early and advanced, previously untreated and recurrent, admitted to the Chemo-surgery Clinic from June 26, 1936 to Sept. 29, 1945 for the six-month group, from June 26, 1936 to April 15, 1943, for the three-year group, and from June 26, 1936 to Oct. 7, 1940 for the five-year group.

TABLE VIII. EFFECT OF SIZE OF BASAL-CELL CARCINOMA ON PROGNOSIS

GROUP	AVERAGE DIAMETER (CM.)	NUMBER OF LESIONS	SUCCESSFUL RESULTS	
			NUMBER	PER CENT
A	Under 1	14	14	100.0
B	1 to 2	15	15	100.0
C	2 to 3	6	5	83.3
D	3 or more	13	10	76.9
All groups		51	47	92.2

*Effect of Size of Lesion on Prognosis.*—The fifty-one basal-cell carcinomas in the determinate group in the sixth-month period were fairly evenly distributed in the four groups as regards size of the primary lesion (Table VIII). No failures occurred in the treatment of lesions in the two smaller-sized groups. One

failure is listed in Group C (average diameter, 2 to 3 cm), and three failures are listed in Group D (average diameter, 3 cm or more) (Examples of lesions in Group D, are shown in Figs. 6 to 8.)

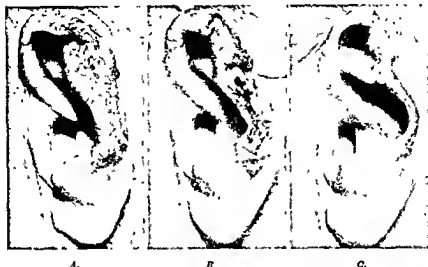


Fig 7—A, Mixed basal- and squamous-cell carcinoma, of Group D. In addition there was a painful radiodermatitis from two courses of roentgen-ray therapy given ten years and six years before. B, Granulations after removal of fixed tissue including cartilage. C, Healed lesion. The patient remains free of cancer after five years.



Fig 8—A, Basal-cell carcinoma of Group D. The lesion arose in the postauricular region and grew into the posterior-auricular fold and onto the posterior surface of the ear. Treatment with caustics had been ineffective. B, Granulation tissue after twelve days. C, Healed lesion showing linear scar. The patient remains free of cancer after three years.

In general, however, large size as such is not an appreciably deterrent factor because the microscopic control afforded by the chemosurgical method makes possible the eradication of very large cancers with all their irregular ramifications. It is more the degree of invasion of underlying vital and inaccessible structures that determines whether or not a successful result is to be obtained.

*Effect of Previous Treatment on Prognosis*—Of the fifty-one patients in the determinate group in the six-month period, thirteen (25.5 per cent) had received previous surgical or radiation treatment. In this group with recurrent lesions the rate of cure was 76.9 per cent as compared to the 97.4 per cent in the group which had received no previous treatment (Table IX). The chief reason for the poorer prognosis in patients with recurrent lesions was the delay occasioned by the ineffective treatment.

TABLE IX. EFFECT OF PREVIOUS TREATMENT OF BASAL CELL CARCINOMA ON PROGNOSIS

	NUMBER OF PATIENTS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
Previously treated	13	10	76.9
Previously untreated	38	37	97.4

The particular usefulness of the chemosurgical method in the treatment of recurrent and often otherwise hopeless cancer is demonstrated by the fact that over three fourths of the patients with recurrent lesions were salvaged.

*Effect of Histologic Grade of Malignancy on Prognosis*—The fifty-one basal-cell carcinomas were grouped according to their degree of invasiveness as determined by microscopic examination. Although there are borderline cases in which it is difficult definitely to classify the lesion as invasive or noninvasive, the majority can be placed readily in one or the other of these categories.

The invasive type exhibits slender strands of basal cells which often assume spindle shapes and which intrude themselves into the interstices of the normal tissues; there is often a strong stroma reaction. (Included in the group of invasive lesions are seven basal-cell carcinomas with some degree of keratinization, two transitional-cell carcinomas, and two mixed basal- and squamous-cell carcinomas.) On the other hand, the noninvasive type of basal-cell carcinoma is made up of regularly shaped cells which are packed closely in rounded or serrated clumps. These clumps are well demarcated from the surrounding stroma which is usually relatively sparse. (Only one lesion of this type exhibited keratinization, and one was a mixed basal- and squamous cell carcinoma.)

In this series of fifty one basal-cell carcinomas there were thirty-eight lesions of the invasive type (74.5 per cent). The rate of cure for these invasive lesions was 89.6 per cent. In contrast, the rate of cure for the thirteen noninvasive lesions was 100 per cent (Table X). The somewhat poorer prognosis associated with invasive carcinoma is due to the ingrowing, destructive nature of the neoplasm, with the consequent more frequent involvement of deep, vital structures. The good prognosis in the noninvasive type is due to the outgrowing,

TABLE X. EFFECT OF HISTOLOGIC GRADE OF MALIGNANCY OF BASAL CELL CARCINOMA ON PROGNOSIS

	NUMBER OF LESIONS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
Invasive	38	34	89.6
Noninvasive	13	13	100.0

relatively nondestructive nature of the lesion; this type may reach a tremendous size and yet cause little destruction of the underlying structures.

It is in the highly invasive lesions that the chemosurgical method is of greatest advantage, because these lesions commonly send out irregular extensions which completely escape detection until located and followed to their terminations by means of repeated microscopically controlled excisions.

*Effect of Site of Origin on Prognosis.*—As with squamous-cell carcinomas, the basal-cell carcinomas arising on the pinna of the ear carry a better prognosis than those arising in more proximal portions of the ear. Thus, the twenty-one lesions which arose on the helix and lobe, in the concha, and on the posterior surface of the ear all were treated successfully (Table XI). On the other

TABLE XI. EFFECT OF SITE OF ORIGIN OF BASAL CELL CARCINOMA ON PROGNOSIS

SITE	NUMBER OF LESIONS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
Helix and lobe	8	8	100.0
Antihelix and crura	—	—	—
Concha	7	7	100.0
Canal and deeper structures	2	0	0.0
Posterior surface	6	6	100.0
Postauricular region	16	15	93.8
Preauricular and tragal region	12	11	91.7
All sites	51	47	92.2

hand, the lesions with a more proximal origin had a lower rate of cure (canal and deeper structures, 0 per cent; postauricular region, 93.8 per cent; and preauricular and tragal region, 91.7 per cent). The reason for the poorer prognosis in the more proximal lesions is the closer proximity to underlying vital or inaccessible structures, the involvement of which renders a cure impossible. For example, one of the lesions which arose deep in the canal or in the middle ear had eroded the bone all around these structures. Although the external portion which extended for 15 cm. in the periosteum of the temporal and parietal bones was successfully removed by means of numerous microscopically controlled excisions, the deep-seated portion which eroded the bone recurred. Another deeply invasive lesion of the canal recurred, as did two far-advanced cancers which arose in the preauricular and postauricular regions, respectively and extensively invaded the temporal bone.

#### THERAPEUTIC RESULTS IN PRECANCEROUS LESIONS OF THE EAR

The chemosurgical method is often of value in the treatment of precancerous lesions of the ear because the microscopic control inherent to the technique makes complete removal certain and also detects early cancerous changes which may not be clinically discernible.

*Senile Keratoses.*—The most common precancerous lesions of the ear are senile keratoses. These are most often found on the portions of the ear most exposed to the rays of the sun, particularly on the helix (Fig. 9) and antihelix. Including two cutaneous horns and one squamous-cell papilloma, there was treated a total of twenty-six senile keratoses. To twenty-two of these the zinc chloride fixative was applied following preparation with dichloroacetic acid,



and in these the diagnoses were microscopically confirmed. Four lesions, which from clinical appearance were quite certainly inactive, were cauterized with dichloroacetic acid.

The patients have been followed for variable periods up to seven and one-half years and no instance of recurrence or malignant change has been observed.

**Seborrheic Keratoses**—Although less common on the ear and less likely to undergo malignant change, seborrheic keratoses were treated with the chemosurgical technique in five patients and with dichloroacetic acid alone in two patients. No recurrences or malignant changes have appeared during observation periods up to four years.



Fig 9—A, Senile keratosis. B, Healed lesion after chemo-surgical excision. The microscopic sections showed much precancerous epithelial hyperplasia but no actual neoplasia.

**Radiation Ulcers.**—The chronic ulcers which occasionally follow intensive roentgen or radium irradiation of lesions on the ear may be classified as precancerous lesions. They may be advantageously treated by the chemosurgical method because the technique allows study of the tissues for possible neoplasia and also enables the efficient removal of the damaged tissues so that prompt healing may occur.

Five patients with radiation ulcers were treated. In three the ulcers healed promptly and there has been no recurrence or malignant change. One patient died of other causes two weeks after treatment. In one patient the radiation ulcer, which was so severe that the entire ear had sloughed off, has not healed after two months due to the slow separation of necrotic bone.

#### DISCUSSION

One important by-product of the work on the chemosurgical method has been the clear demonstration of the frequent occurrence of irregular, small-caliber, clinically undiagnosed outgrowths from the main cancerous mass. This characteristic of cancer has been well illustrated by means of reconstructions by Lathrop<sup>7</sup> and Limberg.<sup>8</sup>

In cancer of the ear these unsuspected outgrowths are frequently encountered. By means of the microscopically controlled excision, characteristic of the chemosurgical method, each of these extensions may be followed accurately to its termination. This explains the great reliability of the method and also its conservatism.

The results obtained with the chemosurgical treatment of cancer of the ear compare favorably with those obtained with other methods. The best previously published series as regards adequate numbers, adequate statistical presentation, and excellence of results is that of Magnusson<sup>9</sup> of the *Radium-hemmet* in Stockholm. From his protocols it was determined that at three years the rate of cure for carcinoma of the ear was 76.2 per cent. In the present series the rate of cure at three years for basal- and squamous-cell carcinoma was 80.6 per cent. This record was attained despite the fact that in this series recurrent lesions constituted 32.3 per cent of the total whereas in Magnusson's series only 22.1 per cent of the lesions were recurrent. The distribution of the lesions as regards size was essentially the same in both series.

The conservatism of chemosurgical excision of cancer of the ear is important if plastic reconstruction is contemplated. Any portion of the ear which can be preserved is likely to be useful in this organ in which cartilaginous support is so important. Moreover, following chemosurgical treatment the tissues are healthy and well vascularized and do not present the difficulties sometimes encountered with irradiated tissues.

Since all cartilage damaged in the process of chemosurgical treatment is promptly removed there is no danger of perichondritis and intractable ulceration such as sometimes follows radiation therapy of cancer of the ear.

Lesions recurrent after roentgen or radium therapy (Fig. 7) constitute prime indications for chemosurgery because they are notoriously insensitive to further irradiation and are difficult to excise surgically because their exact extent is difficult to estimate accurately.

There was no operative mortality in this series. One patient died from coronary thrombosis, four days after treatment, and one died from hemorrhage, two months after treatment, due to carcinomatous invasion of the jugular vein. In neither case could these deaths be attributed to the chemosurgical procedures. In consideration of the advanced age and poor health of many patients with cancer this essential lack of operative mortality is a definite advantage.

Since a special clinic with specially trained personnel is essential to the most effective use of the chemosurgical technique, it is suggested that the method had best be practiced as a specialty.

#### SUMMARY AND CONCLUSIONS

The chemosurgical technique as used in the excision of cancer of the ear is described, and the therapeutic results in a series of 167 cases are analyzed.

The rates of cure in the series of patients with squamous cell carcinoma of the ear were: 80 per cent at six months or more, 74.2 per cent at three years

or more, and 64.3 per cent at five years or more. The primary lesion was eradicated in 92 per cent of the patients.

The rates of cure in the series of fifty-five patients with basal-cell carcinoma of the ear were: 92.2 per cent at six months or more, 87.1 per cent at three years or more, and 81 per cent at five years or more.

The reliability and the conservatism of the method are both due to the systematic microscopic control of excision afforded by the chemosurgical technique.

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## SUCCESSFUL SUTURE OF THE ABDOMINAL AORTA FOR ARTERIOVENOUS FISTULA

LIEUTENANT COLONEL NORMAN L. FREEMAN<sup>\*</sup> AND LIEUTENANT COLONEL  
AMBROSE H. STORCK,<sup>†</sup> MEDICAL CORPS, ARMY OF THE UNITED STATES  
(From the Vascular Surgical Center, DeWitt General Hospital, Auburn, Calif.)

**A**RTERIOVENOUS fistula involving the abdominal aorta and vena cava is rare since patients generally succumb to the initial massive hemorrhage. Makins<sup>1</sup> reported two patients who survived wounds of the abdominal aorta for several weeks. Even if the patient recovers from the initial loss of blood, the short-circuiting of the circulation immediately places such a strain on the heart that early cardiac failure occurs.

Pemberton, Seefeld, and Barker<sup>2</sup> have recently reported the successful repair of the abdominal aorta for an arteriovenous fistula. In a review of the literature they were unable to find any previously reported case in which the patient had survived a reasonable length of time after surgical repair to furnish evidence that the operation had been successful. The present case, which was briefly reported in discussion of their paper, is apparently the second patient in whom a successful repair of the abdominal aorta has been performed.

### CASE REPORT

The patient was a 25-year-old infantry soldier who was wounded on Okinawa May 14, 1945. A .25 caliber bullet entered the abdomen three inches below the ensiform cartilage just to the right of the midline and passed out through the back at the level of the second lumbar vertebra. He was immediately paralyzed below the waist. A laparotomy was performed on the day of injury and a large retroperitoneal hematoma was found. The patient stated that he was told that numerous veins were tied off. The abdomen was closed without drainage. Ten days after injury the patient was transferred to another hospital and roentgenograms were taken which disclosed several fracture lines in the spinous process of the second lumbar vertebra, radiating through the lamina without displacement or separation. On the fifteenth day after injury, a laminectomy was performed and the comminuted fragments of the spine at the first and second lumbar vertebrae and the lamina of the second lumbar vertebra were removed. The underlying dura was found to be compressed and lacerated and three of the roots were found to be severed. Following this operation there was considerable return of function in the lower extremities. On the fifth postoperative day, he developed swelling of the right leg, and a diagnosis of thrombophlebitis was made. The swelling subsided in a few days.

Six weeks after the original injury, the patient complained of some epigastric pain and, on examination, a pulsating mass with intense thrill was found to be present in the upper abdomen. A diagnosis of aneurysm of the abdominal aorta was made and the patient was evacuated to the Zone of the Interior. Upon admission to the Debarcation Hospital, it was noted that the blood pressure was 150/60. The hemoglobin was 72 per

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<sup>\*</sup>From the Department of Surgery, University of California Medical School, San Francisco, Calif.

<sup>†</sup>From the Department of Surgery, Tulane Medical School, New Orleans, La.

†This patient was originally admitted to the Vascular Surgical Section but, because of the associated lesion of the spinal cord, was transferred to the Neurosurgical Section. The urological problems which the case presented were managed by Lieutenant Colonel Donald C. Malcolm. We are also indebted to Lieutenant Colonel Richard B. Capps, Chief of the Medical Branch, for advice in the postoperative care.

or more, and 64.3 per cent at five years or more. The primary lesion was eradicated in 92 per cent of the patients

The rates of cure in the series of fifty-five patients with basal-cell carcinoma of the ear were: 92.2 per cent at six months or more, 87.1 per cent at three years or more, and 81 per cent at five years or more.

The reliability and the conservatism of the method are both due to the systematic microscopic control of excision afforded by the chemosurgical technic.

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initial injury, the patient complained of some abdominal discomfort and vomited. Examination at this time disclosed the mass to be approximately 6 cm. in diameter. Both the pulsation and the thrill were more apparent. Gastrointestinal x ray examination failed to reveal any extrinsic mass producing pressure upon the pylorus or duodenum. The cardiac consultant noted a definite increase in the size of the liver with an increase in the pulse rate, and felt that the patient was showing evidence of cardiac strain. Because of the possibility of cardiac damage and the increase in the size of the aneurysm, it was decided not to delay further, but to subject the patient to operation.

The operation was carried out under intratracheal ether oxygen anesthesia. A right paramedian incision was made from the xyphoid to just below the umbilicus. Numerous dilated veins were encountered in the subcutaneous tissues. On opening the peritoneum, a large pulsating mass was found beneath the gastrohepatic omentum. A puckered scar was present near the border of the liver on the right side, which probably represented the point of entrance of the rifle bullet. The veins of the portal system did not appear to be dilated. The hepatic, common, and cystic ducts were readily visualized and appeared to be pushed forward by the pulsating mass which occupied the posterior aspect of the right upper quadrant. The aneurysm was under considerable pressure and at one point, below and slightly mesial to the gall bladder, the thrill of the arteriovenous fistula was most easily palpable. Compression at this point obliterated the thrill, but this maneuver appeared to produce an increase in the intraaneurysmal pressure. The round ligament of the liver and some adhesions were divided. An attempt was made to visualize the artery entering the aneurysm by division of the gastrohepatic omentum. It was still not possible to localize the opening of the artery into the aneurysm. Only by pressure on the aorta at the hiatus of the diaphragm was it possible both to obliterate the thrill and to cause the aneurysmal sac to collapse. The aorta was, therefore, exposed at this point by dividing some of the fibers of the diaphragm and was encircled by a No. 10 rubber catheter which was fitted to a Bethune tourniquet. Attempt at exposure of the aorta through the root of the mesentery beneath the transverse colon was unsuccessful because of the dilated veins in this region.

The peritoneum and transversalis fascia were then incised from within the abdomen just to the left of the midline, and by separation of these structures from the underlying muscles it was possible to expose the anterior surface of the psoas muscle and the vertebral column. By this procedure, the spleen, descending colon, pancreas, left kidney, and intestines were reflected to the right and the abdominal aorta was readily exposed as it lay on the anterior surface of the lumbar vertebrae. Many large veins were divided and ligated. The tissues about the aorta were thickened and edematous and there was some discoloration present indicative of old hemorrhage. The abdominal aorta was encircled by a segment of rubber tubing just proximal to the origin of the inferior mesenteric artery. It was then exposed just above the origin of the left renal artery and was again encircled by a piece of tubing. Compression of the aorta by this piece of tubing caused the sac to collapse. An additional section of tubing was placed about the left renal artery. With the proximal end distal aorta and left renal artery included, the inflammatory tissues surrounding the aorta at the site of the fistula were excised and the aorta was finally cut away from the aneurysm at this location. The opening into the aorta measured  $\frac{1}{2}$  inch in length. It was closed by a transverse running stitch of No. 000 Deknatel, which had previously been passed through sterile mineral oil. Bleeding from the sac was only moderate and was readily controlled by digital pressure. This opening was closed by a running stitch of No. 000 silk. At the conclusion of this procedure, the segments of tubing around the distal aorta, left renal artery, and then the proximal aorta were released. Good pulsation, expansile in character, was apparent in the aorta below the suture line. No bleeding took place. Two Penrose drains were inserted through a stab wound below the left costal margin into the region of the left lumbar gutter and the abdomen was closed. Fig. 2 illustrates the location of the fistula.

The operation lasted just under eight hours. During this time the patient received a continuous transfusion of 3,000 c.c. of whole blood and 500 c.c. of normal saline solution. When the abdominal aorta was occluded the blood pressure increased from 118/70 to 210/100. The pulse rate increased from 130 to 160, and the neck veins became markedly distended.

The tourniquet was left in place for one hour and forty minutes. Upon release of the rubber tubing, the systolic pressure dropped to 50, but within 30 minutes it rose to 110/80 and the pulse was 140. Immediately after operation, a strong femoral pulse was palpable and within one hour the extremities were warm and dry and the pulse at the wrist was of good volume. He was placed in an oxygen tent and suction was connected to an indwelling Levine tube. By the following morning, the abdomen was flat and peristalsis was present. The patient was conscious and alert. Because of persistent low blood pressure and a rapid weak pulse, he was given another blood transfusion, and penicillin and sulfadiazine were administered. Due to urinary suppression, the sulfadiazine was discontinued after the administration of 7 Gm. in the first thirty-six hours.



Fig. 7

Impaired renal function presented a serious complication. During the first forty-eight hours, in spite of receiving 3,500 cc. of 5 per cent glucose in water and 1,000 cc. of 5 per cent glucose in saline solution, the patient passed only 200 cc. of urine. The blood pressure following the transfusion increased to 160/90. The elevation of the nonprotein nitrogen following operation is shown in Table I.

TABLE I. CHEMICAL CONSTITUENTS OF THE BLOOD

DATE	NONPROTEIN NITROGEN	BLOOD UREA NITROGEN	CITICINIC	CARBON DIOXIDE	SERUM PROTEIN
July 27	33.7				
Aug 14	34	18.7			7.1
Sept 27		Operation			
Sept. 29	111.6		52.2	60.4	6.48
Sept 30	116				
Oct 1	116	80.9	511		5.39
Oct 3	120	91	591		5.75
Oct 5	107		572	59.3	6.48
Oct 9	70.5		568	61.9	
Oct 13	63.1				
Oct. 16	40.5				

For the first week, treatment consisted chiefly of continuous oxygen therapy, decompression of the upper gastrointestinal tract by nasal suction, and the moderate administration of intravenous fluids just sufficient to balance the amount lost through the gastrointestinal tract, kidneys, and insensible loss of water. Three days after operation, the venous pressure in the right antecubital vein was 12.6 cm. of saline solution. The patient was feeling well except for superficial erosions of the mouth and lips and lack of appetite. The blood pressure was consistently 170/40. Six days after operation, ophthalmologic examination revealed a remarkable generalized narrowing of the retinal arterioles throughout all divisions. In many of the vessels, there were variations in caliber indicative of focal spasm. No signs of sclerosis were noted, no exudation, hemorrhages or edema.



FIG. 3

A diagnosis of acute retinal angiospasm was made. Because of persistent anorexia and sore mouth, the patient refused to eat so that on the tenth postoperative day a nasal tube was passed and he was given high caloric feedings by continuous drip for thirty-six hours; 1,500 cc. of fluid containing approximately 1,800 calories were administered. He tolerated this feeding very well and his general condition improved rapidly. The nonprotein nitrogen of the blood dropped as the volume of urinary excretion increased. The wound healed without complications.

The day after operation, the patient noted that he was unable to dorsiflex the left foot. Neurologic examination showed that there was a definite increase in the neurologic disturbances noted prior to operation. In addition to the foot drop on the left side, the area of anesthesia had increased and there was a decrease in the bladder tone. For the first two months after operation, he complained of severe burning pain in both feet, but



this condition suddenly cleared up and there was a concurrent improvement in the motor power.

Evidence of renal damage persisted for several weeks with a constantly low specific gravity of the urine and persistent mild hypertension, and, even six weeks after operation, the ophthalmologic examination revealed moderate generalized narrowing and increased tortuosity of the retinal vessels. Excretory urograms demonstrated a good concentration on both sides without evidence of renal abnormality. As shown in Fig. 3, there was a defect in the laminae between the second and third lumbar vertebrae at the site of the original fracture.

From the location of the injury to the spinal column it seems likely that the laceration in the aorta was just below the origin of the right renal artery.

At the end of two months after operation he was able to stand, first with crutches, and finally was able to walk with the assistance of two canes. He was then transferred to another General Hospital. Eight months after operation it was reported that the patient had shown no evidence of recurrence of the fistula. He had recovered sufficiently from the spinal cord injury to be able to walk with the help of one cane.

#### COMMENT

The presence of a fistula between the abdominal aorta and vena cava leads, generally, to rapid heart failure and death. The absence of this complication in our patient was probably due to the intervention of a large aneurysmal sac between the compound vessels. The aneurysm, which lay behind the vena cava, displaced this structure forward and so compressed it as to hinder the ready flow of blood back to the right heart. The dilatation of the superficial abdominal veins observed before operation is in keeping with this explanation. It is possible that the onset of swelling of the right leg noted ten days after injury was due to interference of return flow of blood from the lower extremities rather than to an attack of thrombophlebitis.

The increase in the paralysis of the pelvic structures and lower extremities following operation was not surprising in view of the fact that the abdominal aorta was completely occluded for 105 minutes. Paralysis of the hindquarters has been observed in dogs by Blalock and Park<sup>3</sup> after complete occlusion of the aorta for a period of forty to fifty-five minutes. Whether the neural damage in our patient was due to impaired circulation to the spinal cord and cauda equina or due to temporary ischemia of the distal nerves would be hard to say, but the involvement of the nerves to the bladder suggests the former explanation. The rapid improvement which was observed two months after operation indicates a favorable prognosis.

The second postoperative complication was the temporary suppression of kidney function associated with hypertension. This complication was probably due to the renal ischemia produced by occlusion of the abdominal aorta above the renal arteries. It was associated with marked vasospastic changes in the eye grounds and nitrogen retention. With resumption of renal function at the end of two weeks, this hypertension subsided. The final urine concentration test, which was done two months after operation, showed an ability to concentrate to 1018. The excretory urogram was also quite satisfactory, but it is quite possible that some permanent damage to the kidneys has been sustained. In the case reported by Alexander and Byron<sup>4</sup> on resection of a segment of the thoracic aorta, hypertension with severe retinal angiospasm, exudates, and hemorrhages proved a late serious complication. Persistent

hypertension with cardiac hypertrophy was also noted in the case reported by Pemberton, Seefeld, and Barker.<sup>2</sup>

At the time of operation considerable difficulty was experienced in locating the arterial communication with the fistula. Reflection of the duodenum with exposure of the anterior surfaces of the aorta and vena cava was the method of exposure employed by Pemberton and associates but the aneurysmal sac in their patient lay to the left of the aorta. Since in our patient the sac appeared to lie between the aorta and the vena cava this approach could not be used. It was only after retroperitoneal exposure of the anterior surface of the psoas muscle and the lumbar vertebrae through displacing the abdominal contents from the left lumbar gutter that the abdominal aorta could be readily exposed. It was then possible to visualize the entire length of this structure from the diaphragm to its bifurcation.

Transvenous suture of the opening between the aorta and vena cava was used by Pemberton and co-workers. This technique is known as the Matas-Bickham<sup>3</sup> operation. Although frequently valuable, it has the disadvantage of not permitting inspection of the entire arterial wall. Arterial aneurysms have been known to develop after this procedure if there happens to be an additional weakened point in the arterial wall. Closure of an arteriovenous fistula leads to a marked increase in blood pressure within the artery at the site of the fistula.<sup>4</sup> If the wall close to the former communication is defective it may give way, leading to the formation of an aneurysm. Complete dissection of the artery from the fistula permits thorough examination so that other damaged portions of the wall will not escape notice. In a series of cases to be reported<sup>5</sup> we have found it useful to excise the damaged portion of the arterial wall and close the defect transversely.

#### SUMMARY

The present case is the second successful suture of the abdominal aorta for an arteriovenous fistula to be reported. A complicating factor was the partial paraplegia resulting from concurrent gunshot wound of the spine. Operative approach to the abdominal aorta through the retroperitoneal space was employed. Increase in the extent of the neurologic damage and temporary renal failure with hypertension and retinal angiospasm were noted in the postoperative period.

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## EVALUATION OF THE BASAL VASCULAR TONE TEST AS AN INDICATION FOR SYMPATHECTOMY IN THE TREATMENT OF SURGICAL LESIONS OF THE MAJOR ARTERIES

CAPTAIN E. W. RICTOR, MEDICAL CORPS, ARMY OF THE UNITED STATES

(From the Vascular Surgical Section, DeWitt General Hospital, Auburn, Calif.)

IN THE treatment of patients with aneurysms, arteriovenous fistulas, and obliteration of major vessels following trauma, the degree of development of collateral circulation is often the deciding factor which determines the outcome. Although the mechanism of the formation of collaterals is still not fully understood, it is recognized that vasoconstriction, through activity of the sympathetic nervous system, may interfere seriously with the supply of blood to the part. Lumbar sympathectomy, repeated injections of procaine into the region of the paravertebral sympathetic ganglia to induce temporary paralysis of vasomotor tone, or the paravertebral injection of alcohol to produce a longer lasting vasomotor release have been advocated in the treatment of these arterial lesions. Sympathectomy has even been recommended by Learmouth<sup>1</sup> as a prophylactic measure in all cases in which ligation of the major artery to an extremity is anticipated.

It is well recognized that, after ligation of arteries in certain anatomic locations, the collateral blood supply is generally quite adequate to care for the metabolic needs of the tissues. For example, following ligation of the superficial femoral artery, the incidence of gangrene or vascular disturbances is minimal, whereas ligation of the popliteal artery is followed by a more serious disturbance of the peripheral circulation. The extent of development of collateral circulation in the presence of an arteriovenous fistula is admittedly better than that observed in the presence of a surgical lesion involving the artery alone. The location of the lesion and the physiologic reactions which it produces are, therefore, important factors in estimating the prognosis in any given case. Even given the same anatomic location and equal disturbance of the main arterial supply, a considerable variation is noted in the degree of vascular insufficiency from one patient to the next. These differences may be ascribed to variations in the facility with which the collateral circulation is developed. It has been shown both experimentally and clinically that paralysis of vasoconstrictor impulses facilitates the development of these collaterals. It is my belief that sympathectomy should be reserved for those patients in whom an increased vasomotor tone can be demonstrated. The question arises as to how best to select those patients for sympathectomy in whom increased vasomotor tone is preventing adequate development of collateral circulation.

The first attempt to study quantitatively the vasomotor tone in man was made by Brown.<sup>2</sup> He noted the ratio between the rise in mouth temperature and the rise in temperature of the extremities following the administration of

typhoid vaccine. Morton and Scott<sup>3</sup> used anesthesia, either general, local, or spinal, and White<sup>4</sup> was the first to use paravertebral procaine injections in order to inhibit vasomotor tone. Gibbon and Landis,<sup>5</sup> by the use of heat applied to the unaffected extremities, obtained a rise in the temperature of the digits. Since vasoconstriction is a normal physiologic response to cold, these tests, although useful in determining the degree of organic arterial occlusion, do not serve to estimate the degree of vasoconstriction which is present. A normal individual, when exposed to a cold environment, will develop vasoconstriction and the skin temperature, especially of the extremities, will fall to a low level. Collier and Maddock<sup>6</sup> have called attention to this fact and have warned against using the term vasospasm for a normal physiologic reaction. After release of vasomotor tone in such a normal individual, either by typhoid vaccine, anesthesia, or reflex vasodilatation, the peripheral skin temperatures will rise to normal high levels. These tests then are useful simply in ruling out organic vascular occlusions. They do not tell the degree of vasomotor activity with which the patient is responding. Considerable differences are observed in the study of the peripheral skin temperatures in any group of patients when exposed to the same environmental conditions. These differences may be related to the basal metabolic rate.<sup>7</sup> White and Smithwick,<sup>7</sup> on the basis of skin temperature curves of individuals exposed to cold, have separated patients into "hot-handed" and "cold-handed" types. The possibility of using these variations in temperature of the digits on exposure to cold as an index to the vasomotor tone of the individual patient has been suggested by Naide and Säyen.<sup>8</sup> In an analysis of the results obtained in 172 patients with the vasodilatation test they were able to group their patients into various types depending upon the skin temperature responses which they observed. Subsequently,<sup>9</sup> they reported that it was necessary simply to observe the skin temperature response of the finger tips during the cooling period in order to classify patients into two basic groups of high and low vascular tone. They regarded the individual as having a high vascular tone "if the hands are cool (below 25° C) fifteen minutes after the patient has been in a constant-temperature room at 20° C unclothed except for a light gown. If, on the contrary, the hands remain warm (25° C or above) after this same exposure, the patient is in a low vascular tone group."

According to the results obtained from this test, Naide and Säyen<sup>8</sup> analyzed the effectiveness of the development of collateral circulation in seventy patients with occlusion of the femoral or popliteal artery which resulted either from arteriosclerosis, thromboangitis obliterans, or embolism. They noted that 88 per cent of the patients with a low vascular tone developed an excellent collateral circulation following major arterial occlusion. On the other hand, in the patients with a high degree of vascular tone, only 34 per cent developed an adequate collateral circulation. Since the development of collateral circulation following surgical lesions of the major arteries is of prime significance in determining the ultimate outcome, it seemed to us that this test might afford a suitable guide to determine which of the patients should be subjected to sympathectomy. The present investigation has been carried out in an endeavor

to evaluate the significance of the "basal vascular tone" test described by Naide and Säyen<sup>9</sup> as an indication for sympathectomy in the treatment of surgical lesions of the major arteries.

There are clinical evidences of increased vasomotor tone such as cyanosis, sweating, and constricted veins which were used by Freeman and Montgomery<sup>12</sup> in the selection of cases with intermittent claudication for sympathectomy. These clinical signs of increased sympathetic tone were used in the present investigation to separate patients into two groups, those exhibiting high and those exhibiting low vasomotor tone. The results of the basal vascular tone test were then compared with the impression obtained on clinical examination of the patient. The ultimate outcome in each patient served to assess the validity of the test in comparison with the clinical impression. This outcome was based on the degree of circulatory impairment, shown particularly by intermittent claudication, which followed ligation of the major artery supplying the extremity.

#### PROCEDURE

Measurements of skin temperature were made with the aid of a galvanometer in a constant-temperature room at 20° C. and 40 per cent humidity. The tests were made in the early morning during the summertime when the environmental temperature was comfortably cool. The patients were in a basal resting state, having omitted breakfast. No smoking was allowed before taking the test. The digital skin temperature was measured at the start of the test and every ten minutes for the succeeding hour. The values of the skin temperature readings obtained thirty minutes after the patient was admitted to the constant-temperature room served as a final reading.

#### RESULTS

Studies were completed on forty-five patients suffering from surgical lesions of the major arteries. Of these, twenty-five patients were studied before operation on aneurysms or arteriovenous fistulas. An additional seventeen patients were studied after the main artery to the extremity had been ligated in the course of operations on arterial lesions. There were three patients who were studied in whom thrombosis of an artery had developed following trauma or in whom the major artery had been ligated shortly after injury. Of the forty-five patients, arterial repair was performed at the time of operation on the vascular lesion in eleven. In an additional three patients, it was found at operation that the major artery to the extremity was not the one involved. In these fourteen patients, although it was possible to compare the impressions derived from examination with the results of the test, it was not possible to judge the relative significance of the two methods of evaluation by subsequent events since the continuity of the main artery was not interrupted. In the remaining thirty-one patients it was possible to compare impressions gained by clinical observations and the indications supplied by the basal vascular tone test and to judge the relative merits of the two methods by the final outcome.

The results of the test were in agreement with the clinical impression in thirty-two of the forty-five patients. Of the thirteen cases in which there was

disagreement it was possible by analysis of the end results in ten patients to compare the significance of the two methods of selection. Clinical judgment was found to be superior to evaluation by the basal vascular tone test in eight of the cases. According to the test, seven of these patients had normal or low vascular tone. Yet clinical signs indicated abnormal vasoconstriction. In several instances in which the test was clearly in disagreement with the clinical observations it was repeated, but the results were the same. In spite of the findings of the test, sympathectomy was performed in six of the seven patients with excellent results. In the remaining case sympathectomy was advised but was not accepted. Persistence of intermittent claudication in this case after excision of a superficial femoral arteriovenous aneurysm supported the belief that the collateral circulation was slow to develop.

The test for basal vascular tone proved to be superior to clinical appraisal in only two patients. In one of these individuals persistent symptoms of intermittent claudication suggested that sympathectomy should have been performed even though there was no clinical evidence of abnormal vasoconstriction. The other patient developed no symptoms referable to vascular insufficiency even though there was clinical evidence of increased vasomotor tone. The fact that the arterial lesion in this patient was situated in the midfemoral region may have facilitated the development of collateral circulation in spite of abnormal vasoconstriction.

In Table I is shown a summary of the significance of the methods employed in the determination of vascular tone in selection of cases for sympathectomy. Six patients who showed evidence of abnormal vasomotor tone by each test were not subjected to sympathectomy for various reasons. Vascular insufficiency persisted in these patients supporting the validity of the criteria. On the other hand, in four patients who also showed evidence of increased vasoconstriction and in whom the test indicated a high basal vascular tone, no symptoms of vascular insufficiency developed even though sympathectomy was

TABLE I

	VALIDATION BY SUBSEQUENT EVENTS		EVALUATION NOT POSSIBLE BECAUSE OF ARTERIAL REPAIR OR NONSIGNIFICANT ARTERY	TOTAL CASES
	YES	NO		
Basal Vascular Tone Test				
High, sympathectomy	12	-	8	20
High, no sympathectomy	6	4	2	12
Low, sympathectomy	-	6	2	8
Low, no sympathectomy	2	1	2	5
Total	20	11	14	45
Clinical Evidence of Vasoconstriction				
High, sympathectomy	13	-	10	23
High, no sympathectomy	6	4	2	12
Low, sympathectomy	-	-	-	-
Low, no sympathectomy	2	1	2	5
Total	21	5	14	40



## SUMMARY

Vasoconstriction appears to interfere with the development of collateral circulation following surgical lesions of major arteries. Sympathectomy is indicated in those patients in whom increased vasomotor tone is present. The basal vascular tone test of Naide and Sayen<sup>9</sup> was compared to the clinical impressions obtained on physical examination in forty-five patients who had sustained injuries to the major arteries. The validity of the test or clinical impression was judged by the subsequent course of events. The test was in agreement with the clinical findings in thirty-two of the forty-five patients. When there was disagreement, clinical judgment appeared to be superior to the test in the majority of cases. In order to explain the discrepancy between the results reported here and those of Naide and Sayen<sup>9</sup> it is suggested that abnormal vasoconstriction may be induced by local trauma and that this segmental arterial spasm may be quite independent of the general vasomotor tone.

I wish to express my sincere gratitude to Major Norman E. Freeman, chief of the vascular surgical section, for his assistance and guidance in preparing this study.

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# THE FLUORESCIN WHEEL TEST FOR COLLATERAL CIRCULATION IN THE PREOPERATIVE EVALUATION OF PATIENTS WITH ANEURYSMS AND ARTERIOVENOUS FISTULAS

CAPTAIN THEODORE B. MASSELL, MEDICAL CORPS, ARMY OF THE UNITED STATES

(From the Vascular Surgical Section, DeWitt General Hospital, Auburn, Calif.)

## INTRODUCTION

ANEURYSMS of major peripheral arteries, although rare in civilian practice are frequently encountered in military surgery. Some lesions involve an artery alone but the majority are associated with an arteriovenous fistula. Quadruple ligation of the constituent arteries and veins and excision of the fistula are usually performed. Ischemia of the tissues distal to the ligation is prevented by adequate blood flow through collateral vessels. Consequently, it is important to have assurance, prior to operation, that the collateral blood supply is sufficient for the needs of the peripheral tissues.

## CLINICAL OBSERVATION

It is possible to arrive at a general estimate of the state of the collateral circulation from the history and physical examination of the patient. The duration of the presence of the aneurysm is significant in that adequate collaterals are rarely present in less than two months after injury. It is important to distinguish simple arterial aneurysms from arteriovenous fistulas inasmuch as the latter condition is generally associated with a much more rapid and abundant development of collateral channels than is the former.

The textbooks on surgical anatomy describe the so-called safe and unsafe sites for arterial ligation. While the anatomic principles concerned are true, there is actually far more variation in the size and even the location of major arterial branches than is commonly recognized. Accurate localization of an aneurysm in relation to some important collateral branch, for instance the subscapular or profunda femoris artery, may often be achieved by arteriography.

As Holman<sup>1</sup> emphasized, the chief stimulus to the development of collateral circulation in the presence of an arteriovenous aneurysm is the ease of flow through the site of decreased resistance at the fistula. The larger the fistulous opening, the more developed will be the collateral flow. For any given anatomic location, compression of a large fistula causes a greater rise in diastolic blood pressure and more slowing of the pulse rate than that observed with a small communication. Weak or absent pulses and low oscillographic readings distal to an arteriovenous aneurysm, two or three months after injury, suggest a large fistula whereas normal pulses and full oscillations are associated with a small opening. Likewise intermittent claudication in a patient with a femoral or a popliteal arteriovenous aneurysm is suggestive of a large communication.

## MATAS MOSZKOWICZ TEST

Although clinical observation alone provides a good estimate of the state of the collateral circulation, some more exact method is desirable in most cases. In 1914 Matas<sup>2</sup> described a test for collateral blood flow which he attributed to Moszkowicz. According to this technique the involved artery is compressed just above the aneurysm by a special clamp until all blood flow through the sac is abolished. With the extremity elevated, an Esmarch bandage is firmly applied from the distal part of the extremity up to the aneurysm. The limb is kept emptied of blood in this way for from five to ten minutes. Then, with the compressor maintained in place, the Esmarch bandage is rapidly removed and the limb is brought to the horizontal position. The blood returns to the toes or fingers until a flush is produced. If the collateral circulation is good the flush will reach the distal parts within one minute. If more than three minutes is required, arterial ligation is contraindicated.

In using the Matas Moszkowicz test, the results have been variable and the significance in preoperative selection of cases has been questionable. Interpretation of the end point has varied with different observers. The compressor may slip as the position of the extremity is changed so that blood may flow through a supposedly occluded artery. On more than one patient one observer has found the collateral time to be less than one minute on one day, only to have another observer on the same patient find an interval of over three minutes a few days later.

## FLUORESCIN WHEEL TEST

Recently, Neller and Schmidt<sup>3</sup> described a new technique for the evaluation of the circulation in patients suffering from peripheral vascular disease. They discovered that fluorescein when injected intravenously, would cause brilliant fluorescence at sites of minute trauma in an area where the peripheral circulation was not severely impaired but that no fluorescence would appear if the circulation was inadequate to supply the normal metabolic needs of the tissues. Furthermore, they found that the area of fluorescence corresponded to the wheel component of triple response to injury described by Lewis.<sup>4</sup> These authors then used this test to determine the safe level for amputation of limbs with impending or early gangrene. Although Neller and Schmidt reported their results in only six cases, their method seemed applicable to a study of the collateral circulation in cases of aneurysms and arteriovenous fistulas.

The following technique was employed. The flow of blood through the main artery at the site of the aneurysm was first completely occluded by a modified Matas compressor. The completeness of the occlusion was verified by auscultation before and after the test since a compressor might be tight enough to obliterate the palpable thrill of an arteriovenous aneurysm and yet allow enough blood to pass to produce a readily audible bruit. On the other hand the head of the clamp should be sufficiently small so as not to obstruct important collateral vessels near the aneurysm. A modification of the Matas compressor, which has proved satisfactory, is illustrated in Fig. 1.

With the clamp maintained tightly in place over the aneurysm, a series of parallel scratches was made, at intervals of 6 to 8 cm. on both extremities from

the level of the clamp to the proximal phalanx of the great toe or the middle finger. Ten cubic centimeters of 10 per cent fluorescein in a buffered sodium carbonate solution were injected into the antecubital vein. The room was darkened and the extremities were examined by filtered ultraviolet light. The scratches became brilliantly fluorescent within a few minutes after injection of the dye. The time required for appearance of fluorescence was not significant. The criterion of circulatory adequacy was taken as the lowest level of wheal fluorescence.

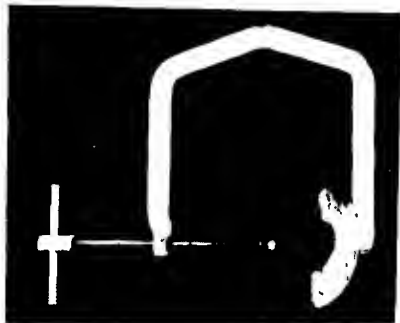


FIG. 1.—A modification of the Matas compressor. The plastic head is applied directly over the aneurysmal opening. A small head is used to avoid occlusion of collateral vessels in the vicinity. The curved surface of the opposite jaw tends to keep the clamp securely in place when the limb is moved.

At first this test was performed without a compressor on seven patients each of whom had previously had a major peripheral artery ligated. The lower extremity was involved in six cases and the upper extremity in the seventh. None of the patients had gangrene but all had symptoms and signs of varying degrees of arterial insufficiency. Two had superimposed vasospasm. In order to establish a standard of normal circulation the level of wheal fluorescence was tested simultaneously on the opposite normal limb in each patient. The results were somewhat surprising in that the lowest level of fluorescence in the normal extremity varied in different patients from the ankle to the base of the proximal phalanx. However, wheal fluorescence reached the same level in both the affected and the nonaffected limb in six cases. In only one patient was there a difference in level between the two sides and then it was only 8 cm., the distance between two scratch marks.

The test was then carried out on twenty-eight patients with traumatic aneurysms. In two patients the artery alone was involved and in twenty-six cases there were arteriovenous fistulas. The results are given in Table I. In each case a Matas flushing test was performed at the same time as the fluorescein wheel test. When the lowest level of wheel fluorescence was the same in both the affected and the normal extremity the collateral circulation was interpreted as good. When the lowest level of fluorescence on the affected side did not extend as far distally as that on the normal limb, but if the difference was less than 8 cm., the collateral circulation was termed adequate. In some instances the intensity of fluorescence was equal on both sides at the next to the lowest level, but on the affected side was fainter at the lowest level. Such circulation is considered adequate rather than good (see Fig. 2, *B*). If the difference in level was greater than 8 cm. the collateral circulation was considered to be poor (Fig. 2, *A*).



FIG. 2.—Types of response with fluorescein wheel test. In *A* the lowest level of wheel fluorescence is just above the mid-calf region on the side of the aneurysm in contrast to *B* in which there is faint fluorescence to the base of the first toe (as on the normal side) although the lowest wheel is fainter than on the control side. The situation in *A* signifies poor collateral circulation that in *B* is considered adequate. If the lowest level on the affected side equaled that on the control in location and brilliance, the collateral supply would be considered good.

The results of the Matas test agreed fairly well with those of the fluorescein wheel test in regard to operability of the patients. In three cases (Cases 1, 2, and 5) in which the flushing time was more than one minute but less than three minutes, wheel fluorescence indicated adequate collateral circulation. Only one of these patients had a major artery ligated. His collateral supply was found to be perfectly adequate after operation. In one patient (Case 20) the Matas flushing time was just short of three minutes but the fluorescein wheel test demonstrated marked inadequacy of collateral blood flow. This patient subsequently was subjected to lumbar sympathectomy. Unfortunately his collateral circulation was not rechecked following this procedure. However, measurements of the intravascular pressure during the operation<sup>3</sup> indicated

TABLE I. STATUS OF COLLATERAL CIRCULATION PRIOR TO OPERATIONS FOR ANEURYSM

CASE NO.	TYPE OF ANEURYSM	LOCATION	COLLATERAL TIME		COLLATERAL CIRCULATION BY WHEEL FLUORESCENCE	MANAGEMENT OF ARTERY AT OPERATION	REMARKS
			MIN.	SEC.			
1	Arterio venous	Radial and ulnar	2	20	Adequate	Reconstruction	Ulnar artery remained patent, radial became thrombosed
2	Arterio venous	Superficial femoral	1	45	Adequate	Reconstruction	
3	Arterio venous	Popliteal	0	45	Adequate	Reconstruction	
4	Arterio venous	Popliteal	0	45	Good	Reconstruction	After lumbar sympathectomy
5	Arterial	Superficial femoral	1	30	Adequate	Ligation	Emergency operation because of increase in size
6	Arterio venous	Popliteal	0	35	Good	Ligation	After lumbar sympathectomy
7	Arterio venous	Popliteal	0	55	Adequate	Ligation	After lumbar sympathectomy
8	Arterio venous	Superficial femoral	0	30	Good	Ligation	After lumbar sympathectomy
9	Arterio venous	Superficial femoral	0	30	Good	Ligation	
10	Arterio venous	Superficial femoral	0	20	Adequate	Ligation	After lumbar sympathectomy
11	Arterio venous	Superficial femoral	0	25	Good	Ligation	Very large fistula
12	Arterio venous	Popliteal	0	50	Good	Ligation	After lumbar sympathectomy
13	Arterio venous	Superficial femoral	0	50	Good	Ligation	
14	Arterio venous	Superficial femoral	0	45	Adequate	Reconstruction	
15	Arterio venous	Popliteal	0	50	Good	Reconstruction	After lumbar sympathectomy
16	Arterio venous	Femoral popliteal	0	15	Adequate	Thrombosis after reconstruction	After lumbar sympathectomy
17	Arterio venous	Superficial femoral	0	30	Good	Spontaneous closure	
18	Arterio venous	Popliteal	0	30	Good	Ligation	Very large fistula
19	Arterio venous	Superficial femoral	0	30	Adequate	Ligation	Very large fistula
20	Arterio venous	Popliteal	2	45	Poor	Reconstruction	Measurements of collateral before sympathectomy
21	Arterio venous	Superficial femoral	0	40	Good	Reconstruction	
22	Arterial	Superficial femoral	0	40	Good	Reconstruction	
23	Arterio venous	Profunda femoris	0	25	Good	Ligation of branch	
24	Arterio venous	Medial inferior geniculate	3	30	Poor	Ligation of branch	After lumbar sympathectomy
25	Arterio venous	Femoropopliteal	Not obtainable		Poor	Ligation	Large collateral close to aneurysm
26	Arterio venous	Femoropopliteal	6	0	Poor	Ligation	Large collateral close to aneurysm
27	Arterio venous	Superficial femoral	0	55	Good	Reconstruction	After lumbar sympathectomy
28	Arterio venous	Superficial femoral	3	10	Poor		Large collateral close to aneurysm

that even after sympathectomy the collateral blood supply was inadequate, thereby confirming the results of the fluorescein wheel test.

On twenty-three patients with satisfactory collateral circulation according to the fluorescein wheel test, nine were classified as adequate and fourteen as good. An attempt was made to relate this difference to the Matas flushing time. However, there seemed to be little correlation. Thus, eight of the patients with good collateral supply showed a flushing time of over thirty seconds and only six had an appearance of color in thirty seconds or less. Although six patients in the termed adequate group required over one-half minute for flushing, there were three patients in whom the time for flushing was thirty seconds or less. The fluorescein wheel results seemed to be more in keeping with the clinical impression in the individual case than did the flushing test.

All but one of the twenty-eight patients who were studied have come to operation. The one patient had a spontaneous closure of an arteriovenous fistula while under observation. The artery has remained patent. In two cases the aneurysm was found to originate from a large branch rather than from the main artery—the profunda femoris rather than the superficial femoral and the medial inferior geniculate instead of the popliteal, respectively. Reconstruction of the injured artery was performed successfully in ten cases. Thus, in thirteen cases cure of the aneurysm has been effected without interruption of the major artery.

In the remaining fifteen patients the enucleation has been carried on through collateral vessels since ligation of the affected artery was necessary in fourteen patients, and one developed thrombosis of the artery at the site of an attempted repair. None of these patients have developed gangrene and in only two was there transitory coolness and paresthesia of the toes. Preoperative examination, both by wheel fluorescence and by the Matas collateral time indicated adequate or good collateral circulation in twelve cases. Three patients showed inadequate collateral supply by the fluorescein wheel test. The collateral time in two cases was over three minutes, corroborating the results of the fluorescein wheel test. In the third patient an accurate flushing time was not obtainable because of a persistent tendency of the compressor to slip when the limb was moved.

Subsequent observation demonstrated that each of those three patients had an abundant collateral circulation, which was, however, propagated through a vessel that branched off the femoral artery just above or below the aneurysm. Consequently, when the Matas compressor was applied over the aneurysm, it also occluded the chief source of collateral blood flow. In each case the femoral artery was ligated and the aneurysm excised without damaging the collateral branches in the proximity. The postoperative results were satisfactory and one patient had a palpable posterior tibial pulse the day after operation.

The case report of one of these patients is given here to illustrate the method of correlating these special tests for collateral circulation with the other clinical findings.

CASE 26.—A penetrating shell fragment wound of the left thigh, Jan. 20, 1945, resulted in an arteriovenous aneurysm of the femoral vessels just above the adductor canal. The patient was admitted to DeWitt General Hospital three months after injury. The only complaints were aching and swelling of the left leg with prolonged weight bearing. Examination revealed a small pulsatile mass with a loud characteristic continuous bruit and thrill of arteriovenous aneurysm. The left foot was still somewhat cyanotic and exhibited pallor on elevation. The posterior tibial pulse was markedly reduced in the affected leg. Occlusion of the aneurysm raised the diastolic blood pressure from 50 to 80 and slowed the pulse rate from 100 to 68.



Fig. 3 (Case 26).—Arteriogram. Arrow indicates large branch of femoral artery arising just above the aneurysm. This important source of collateral circulation was cut off by occluding the aneurysm with a Matas compressor.

Despite clinical evidence of a large communication between the artery and the vein, the collateral time was over three minutes and wheel fluorescences did not appear below the level of compressor on the affected leg. A lumbar sympathetic block produced an excellent rise in skin temperature in the left foot but neither test showed improved collateral circulation.

An arteriogram revealed that a large branch of the femoral artery originated just proximal to the aneurysm (see Fig. 3).

This branch, a major source of collateral circulation, was so close to the fistula that it was impossible to occlude the latter by a Matas compressor without obstructing the

branch at the same time. Consequently, both tests of collateral circulation were incorrect since they required a clamp which obliterated an important portion of the collateral blood supply.

At operation the large proximal branch was isolated and preserved above the site of ligation. Postoperative recovery was uneventful and the patient was able to resume moderate activity without evidence of arterial insufficiency.

#### THE EFFECT OF SYMPATHETIC BLOCK AND SYMPATHECTOMY ON WHEEL FLUORESCENCE

In this series all but two patients had adequate collateral circulation at the time of operation. However, in four cases the fluorescein wheel test indicated inadequate collateral supply at the time of the first observation. A fifth patient seemed to have adequate collaterals according to the level of wheel fluorescence but the Matas flushing time was over three minutes. Two of these patients had a lumbar sympathetic block by the injection of 2 per cent procaine solution into the second lumbar ganglion. While the block was still effective the tests for collateral circulation were repeated. In both cases an improvement in the collateral flow was demonstrated. On the basis of the improved circulation through collateral channels following sympathetic block lumbar sympathectomy seemed indicated. Not only the two patients tested by procaine sympathetic block but the other three (mentioned previously) with inadequate collateral circulation were also subjected to sympathectomy. The results are given in Table II.

TABLE II EFFECT OF SYMPATHECTOMY ON COLLATERAL CIRCULATION

CASE NO.	LOCATION	BEFORE SYMPATHECTOMY			AFTER LUMBAR SYMPATHETIC BLOCK			AFTER LUMBAR SYMPATHECTOMY		
		COLLATERAL TIME		COLLATERAL CIRCULATION BY WHEEL FLORES CENCE	COLLATERAL TIME		COLLATERAL CIRCULATION BY WHEEL FLORES CENCE	COLLATERAL TIME		COLLATERAL CIRCULATION BY WHEEL FLORES CENCE
		MIN	SEC		MIN	SEC		MIN	SEC	
4	Popliteal	3	45	Adequate	1	0	Adequate	0	45	Good
6	Popliteal	5	0	Poor				0	35	Good
7	Popliteal	3	15	Poor				0	55	Adequate
8	Superficial femoral	1	45	Poor	0	25	Good	0	30	Good
12	Popliteal	0	40	Adequate				0	50	Good
15	Popliteal	5	0	Poor				0	50	Good
20	Femoral popliteal	6	0	Poor	5	40	Poor			

It will be noted that four of the five patients were found to have good collateral supply after sympathectomy and the fifth patient was found to have an adequate collateral circulation. The Matas flushing time in each instance was decreased to less than sixty seconds.

Also included in Table II is Case 12 in which there seemed to be adequate collateral supply prior to sympathectomy. The indication for excision of the lumbar ganglia in this instance was the location of the aneurysm low in the popliteal space. Intermittent claudication is frequently severe after arterial ligation at this level even though, as in this case, the collateral circulation



may be sufficient to prevent gangrene. According to the fluorescein wheel test there was a perceptible improvement in the collateral supply after sympathectomy.

In contrast to the effect of lumbar sympathetic block on the criteria of collateral circulation in two patients (Cases 4 and 8), there was no significant improvement in another (Case 26) by either test. This case has been discussed as one of those in which the Matas compressor obstructed a major collateral branch. The effect of sympathetic block was determined before the significance of the large arterial branch was understood and when it was believed that the collateral circulation was actually inadequate. The observation that there was no change in wheel fluorescence after sympathetic block probably saved this patient an unnecessary sympathectomy.

### CONCLUSION

The fluorescein wheel test for collateral circulation has been used in twenty-eight cases. Up to the present time it seems to have the following advantages over the Matas flushing time test:

1. Wheel fluorescence provides a clear and definite end point which is not subject to individual variation depending on the person who performs the test.

2. There is no arbitrary time limit. Comparison is generally possible with the opposite normal extremity. The criterion of normal value is provided in the opposite extremity in each observation.

3. Since the extremity does not have to be moved during the test, there is less danger of error from slipping of the compressor.

4. The fluorescein wheel test takes less time than the Matas collateral time technique and, therefore, is less painful to a hypersensitive patient.

Both tests present three defects:

1. Since both procedures require the use of a Matas compressor they are not applicable in cases in which the compressor cannot be used, either because of the anatomic location of the aneurysm (for example, in the subclavian or the iliac vessels) or rarely because the clamp causes severe pain over a sensory nerve involved in scar tissue at the aneurysm site.

2. As in three cases described previously, the compressor may occlude an important collateral branch in the immediate proximity of the aneurysm. This error may be detected by utilizing the information to be obtained from an adequate physical examination and an arteriogram.

3. Although the collateral circulation may be sufficient to prevent gangrene, ligation of a major artery often results in marked limitation of the patient's exercise tolerance because of weakness in an upper extremity or intermittent claudication in a lower limb. Neither test provides any means of anticipating, prior to operation, just how much activity a patient will be able to enjoy after arterial ligation. In general, claudication seemed more severe in those patients whose fluorescein wheel examination suggested adequate collateral circulation than in those patients whose collateral supply was considered good.

## SUMMARY

Operative cure of an arteriovenous fistula of a major artery frequently necessitates quadruple ligation of the component arteries and veins. It is necessary to know that the collateral circulation is adequate prior to operation. The Matas-Moszkowicz flushing time test of collateral blood flow has been found to give variable results.

A new method of testing collateral circulation has been devised, based on the observations of Neller and Schmidt on wheal fluorescence. The aneurysm is occluded by a Matas compressor. A series of parallel scratches is made less than 8 cm. apart both on the involved and on the opposite extremity. Ten cubic centimeters of 10 per cent fluorescein are injected into an arm vein and the level of wheal fluorescence is examined by filtered ultraviolet light. If the collateral circulation is adequate, the lowest level of fluorescence should not be more than 8 cm. higher on the involved extremity than on the normal control.

Twenty-eight patients with aneurysms have been examined before operation both by this technique and by the Matas-Moszkowicz test. The fluorescein wheal test seems to give a more accurate picture of the state of the collateral circulation than does the flushing time determination.

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# DIRECT MEASUREMENT OF BLOOD PRESSURE WITHIN ARTERIAL ANEURYSMS AND ARTERIOVENOUS FISTULAS

LIEUTENANT COLONEL NORMAN E. FREEMAN,\* MEDICAL CORPS,  
ARMY OF THE UNITED STATES

(From the Vascular Surgical Section, DeWitt General Hospital, Auburn, Calif.)

## INTRODUCTION

IN THE selection of the optimum time for operation on patients with aneurysms and arteriovenous fistulas, numerous tests for the adequacy of the collateral circulation have been devised. With temporary occlusion of the main arterial supply above the aneurysm, the color and temperature of the skin of the distal parts are noted. The peripheral pulses are palpated or oscillographic readings are made to ascertain the presence of collateral vessels. The Matas-Moszkowicz<sup>1</sup> test which depends upon the reactive hyperemia following temporary total circulatory occlusion is perhaps the most reliable and best known of these tests for determining preoperatively the extent of the collateral circulation. These tests have made operations safe. In the past twelve months eighty-eight patients were operated upon at this Vascular Center with resection of the aneurysms or arteriovenous fistulas without the development of a single case of gangrene of the extremity.

Additional tests have been described which foretell at the time of operation the safety of ligation of the major artery. Observation is made of the temperature and color of the skin of the fingers or toes with temporary compression of the proximal artery. The return flow of blood in the accompanying vein is noted immediately after obstruction of the main artery. Probably the most valid sign is pulsation of the distal artery, the so-called Coenen Henle phenomenon, even though the main artery is occluded. In the presence of this sign the adequacy of the collateral circulation is probably well established. Various other procedures have been suggested such as making a small incision in the distal part of the extremity or even exposure of a small distal artery to ascertain whether or not there is a supply of blood to the part. All of these tests are useful, but they are qualitative rather than quantitative. Experience in their use is necessary in order to interpret the results. It was felt, therefore, that some more quantitative test for the adequacy of the collateral circulation was needed so that the surgeon at the time of operation could decide whether or not the main arterial supply to the part could be safely ligated.

Direct measurements of the blood pressure within the aneurysmal sac or distal artery appeared to offer a quantitative measurement of the degree of development of collateral circulation. Such measurements have been made in twenty-three cases of arterial aneurysms and arteriovenous fistulas which have come to operation at this Vascular Center in the past six months. By the use

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\*From the Department of Surgery, University of California Medical School, San Francisco, Calif.

of this technique not only have data been obtained on the development of the collateral circulation, but in addition some facts have been observed in respect to the hemodynamics in these arterial and arteriovenous lesions.

#### TECHNIQUE

A small, three-way stopcock is fitted with short lengths of rubber tubing connecting a 20 gauge needle with a 10 c.c. syringe. To the third arm is attached an aneroid manometer similar to those used with a blood pressure cuff. The manometer is not sterile, but is enclosed in a sterile transparent oiled silk cover. A diagram of the apparatus is shown in Fig 1.

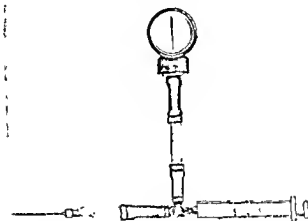


FIG. 1.—Diagram of apparatus used for measuring intravascular pressures in patients with arterial aneurysms and arteriovenous fistulae.\*

After operative exposure of the lesion the component vessels are encircled with pieces of rubber tubing or heavy silk thread. The needle is inserted directly into the artery or into the aneurysmal sac and a few cubic centimeters of saline solution are injected in order to clear the system of blood. The pressure can then be read directly on the dial. Oscillations of the manometer needle, although small, indicate the presence of the intravenous needle within the blood stream. After measurement of the initial pressure, the component vessels are temporarily occluded and variations in pressure following each manipulation are noted. After removal of the needle from the artery or sac, only slight temporary bleeding has been observed in the cases.

#### ARTERIAL ANEURYSMS

*Results.*—Measurements were made of the intra-aneurysmal pressure in twelve cases of arterial aneurysms. The results are summarized in Table I. In the first patient the collateral circulation had been well established.

**CASE 3 (Registry No. 4977)**—A 27-year old corporal sustained a rifle bullet injury of the left axilla in 1935 while in civilian life. There were immediate paralysis and numbness

\*Illustrations throughout this article are through the courtesy of Museum and Medical Arts Service, U. S. Army Medical Museum

TABLE I MEASUREMENTS OF PRESSURES IN ARTERIAL ANEURYSMS

CASE NO.	HOS. FATAL RESULTS	ARTERY INVOLVED	INITIAL PRESSURE	OCCUSION OF PROXIMAL ARTERY	OCCUSION OF DISTAL ARTERY	OCCUSION OF PROXIMAL AND DISTAL ARTERIES	OCCUSION OF PROXIMAL AND COLLATERAL ARTERIES	TREATMENT	RESULT
1	6577	Superficial femoral	90*	80				Intra-arterial closure	Ankle pulses present 3 mo.
2	9493	Popliteal	90*	80				Intra-arterial closure	Ankle pulses present 2 mo.
3	4977	Axillary	110	80				Intra-arterial closure	P.O. normal radial pulse
4	8743	Axillary	64	35	60	40		Intra-arterial closure	Circulation adequate
5	7430	Pulsating aneurysm	110	50			41	Proximal ligation	Slight persistent limp
6	6443	Axillary	75	60			40	Intra-arterial closure	Circulation adequate
7	8061	Superficial femoral	90	44.54 (2 min.)	94			Transverse repair	Normal circulation
8	8561	Popliteal	74*	(consistent AV fistula)				Intra-arterial closure	Circulation adequate
9	2598	Axillary	90	32.45 (3 1/2 min.)				Intra-arterial closure	Temporary ischemia
10	3154	Carotid	110	60.84 (30 sec.)				Excision	Hemiplegia after injury
11	4348	Subclavian	86	32	100			Intra-arterial closure	Circulation adequate
12	4298	Profunda femoris	74	(thrombus in aneurysm)	18			Intra-arterial closure	Normal circulation

\*Pressure measured before operation by direct puncture

of the left upper extremity, but function returned about two months after injury. At the time of examination in March, 1915, there was still some residual weakness of the left hand.

He was inducted into the service Dec. 9, 1912, and assigned to an MP battalion. In June, 1914, because of persistent weakness of the left hand, he was admitted to a general hospital and at that time a small pulsating tumor was discovered in the upper part of the left axilla. The radial pulse was found to be weaker on the left than the right side and the blood pressure was 120/90 on the left side and 150/120 on the right side. A systolic murmur was audible over the tumor. While under observation the mass in the axilla increased in size and accordingly he was subjected to operation on May 31, 1915. The third portion of the axillary artery was exposed and a rubber tube was placed about it. The incision was then extended down below the axilla and the brachial artery was exposed. A second piece of rubber tubing was placed about this artery below the aneurysm. Two large collateral arteries were found leaving the axillary artery above the aneurysm and entering the brachial below the sac. After separating the ulnar and median nerve from the surface of the sac, the intra-aneurysmal pressure was measured. In Fig. 2 are illustrated the conditions found at operation.

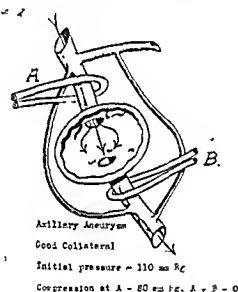


Fig. 2 (Case 3) —Diagram of circulation

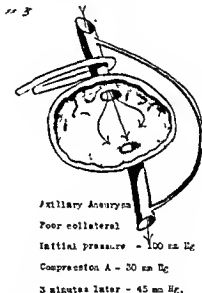


Fig. 3 (Case 9) —Diagram of circulation

The initial pressure was 110 mm. of mercury. Upon compression of the proximal artery the pressure gradually dropped in 15 seconds to 80 mm. of mercury. The blood was then squeezed out of the sac and the constriction applied as well to the efferent artery. When both the artery leading into and the artery leading out of the sac were occluded, the pressure failed to rise within the sac. The aneurysm was then opened and the arteries leading into it were closed from within the sac. Immediately after operation the radial pulse was palpable on the left side, and the patient made an uninterrupted convalescence. The function of the ulnar and median nerves returned rapidly and he was discharged to duty.

*Comment.*—Measurement of the intra-aneurysmal pressure in this case was helpful, both in showing that the collateral circulation was well established and in showing that no other vessels communicated with the sac.

The second patient had received the wound *more recently* and the collateral circulation was poorly established.

**CASE 9** (Registry No 2995).—A 24 year old sergeant was wounded in the left axilla on June 5, 1914, by a .25 caliber rifle bullet. Because of damage to the brachial plexus he was operated upon Sept. 23, 1914, and a neurolysis of the ulnar, median, and radial nerves was performed. At this time an aneurysm of the axillary artery was noted, but no attempt was made to excise it. Following operation there was improvement in the function of the ulnar and median nerves, but complete paralysis of the radial nerve persisted. Moderate signs of circulatory insufficiency were noted, and attempts were made to improve the collateral circulation by compression of the aneurysm. However, this procedure caused so much pain in the hand that it could not be performed adequately. On July 5, 1915, the axilla was again explored and the third portion of the axillary artery was surrounded by a piece of rubber tubing. A schematic diagram of the component vessels is given in Fig. 3.

Upon constriction of the afferent artery the initial pressure of 100 mm. of mercury dropped to 30 mm. of mercury. The pressure within the aneurysm slowly increased so that 1½ minutes later it was at 40 mm. of mercury and 3½ minutes after constriction of the afferent artery the mean pressure was 45 mm. of mercury. The afferent artery below the aneurysm was likewise secured by a piece of rubber tubing. With both arteries occluded the sac was opened and the component vessels ligated from within the sac. Following this procedure the neurolysis was performed on the nerves of the brachial plexus.

Immediately after operation the hand was found to be cold and evanolic, but within a period of three hours circulation returned and the patient made a good recovery. The radial pulse was not palpable two months after operation but there were signs of regeneration of the nerves.

**Comment**—Determination of the intra-aneurysmal pressure in this case revealed that the collateral circulation was poorly established. The rise from 30 to 45 mm. of mercury in the period of 3½ minutes following occlusion of the axillary artery demonstrated, however, that there were collateral vessels present which could dilate sufficiently to care for the metabolic needs of the tissues of the hand.

In the third patient the collateral circulation was well established, but in addition to the main arteries the patient had some collateral vessels emptying directly into the aneurysmal sac.

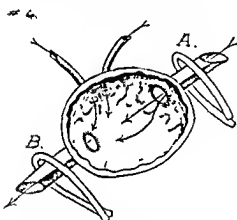
**CASE 11** (Registry No 6643).—A 24 year old sergeant was wounded in the right axilla by a shell fragment on April 9, 1915. He sustained a severe lesion of the brachial plexus and developed a tense, pulsating swelling in the right axilla. He had severe pain and swelling of the hand and forearm. Exploration of the axilla was performed on July 9, 1915, and at that time a large arterial aneurysm was found in the second portion of the axillary artery. After control of the afferent and efferent arteries the pressure within the sac was measured. The initial pressure was found to be 75 mm. of mercury. With compression of the afferent artery the pressure dropped to 60 mm. of mercury. When the efferent artery was also compressed the pressure still remained at 60 mm. of mercury, but upon digital compression of the tissues beneath the sac, it was possible to empty the sac and control the inflow of blood into it. The sac was accordingly opened and two large arteries were found leading into it on the posterior surface. In Fig. 4 is shown the relationship of the collateral arteries to the sac.

These arteries, as well as the openings of the axillary artery, were closed from within the sac. The cords of the brachial plexus were separated from the wall of the sac and the wound was closed. After operation the patient made an excellent recovery, the pain decreased markedly, and some two months after operation there was recovering function of the brachial plexus. At no time was there any evidence of circulatory impairment to the right hand, and the right radial pulse was present after operation.

*Comment.*—Determinations of pressure in this patient not only disclosed that there was good collateral circulation, but also revealed the presence of the additional arteries communicating with the aneurysmal sac.

The results obtained in the cases of simple arterial aneurysms are summarized in Table 1.

In addition to these patients whose pressures were measured at the time of operation, in four additional cases the pressure within the aneurysm was measured by direct puncture through the intact skin before operation. In one patient with an aneurysm of the neck it was demonstrable that the oscillations of the needle could be checked by direct pressure on the common carotid artery at its bifurcation. This patient had developed a hemiplegia immediately following the injury and the demonstration that the pressure within the sac did not drop after occlusion of the common carotid indicated that the internal carotid must have been obliterated at the time of the initial injury. This fact was subsequently borne out at the time of operation.



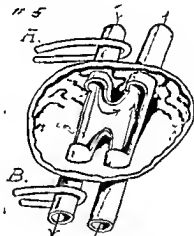
Axillary Aneurysm with tributaries

Initial pressure = 75 mm Hg

Compression A = 60 mm Hg.

A - B = 50 mm Hg.

Fig 4 (Case 6) —Diagram of circulation



Femoral Arteriovenous Aneurysm

Initial pressure = 35 mm Hg

Compression at A = 12 mm Hg. B = 40 mm Hg

Fig 5 (Case 11) —Diagram of circulation

In a second patient who was suffering from an arterial aneurysm of the superficial femoral artery which had recently started to expand, the pressure within the sac was found to be well maintained after digital occlusion of the superficial femoral artery above the aneurysm. After insertion of the needle he developed severe pain in this thigh, and the ankle pulses, which had previously been present, disappeared. It was felt that thrombosis had occurred within the sac and this fact was confirmed at the time of operation. This patient is the only individual in the series who developed any complication following needling of the aneurysmal sac.



The high initial pressure, 90 mm. of mercury, observed in this patient with a pulsating hematoma which was in the process of expanding accounts for the severe pain, toxicity, and damage to surrounding structures characteristic of such lesions. A similar high pressure was observed in another patient (Case 2) with a pulsating hematoma of the popliteal space. The danger of nerve damage and occlusion of collateral circulation, both arterial and venous, from such unchecked pressure makes early operative intervention necessary.

Simultaneous occurrence of an arterial aneurysm and an arteriovenous fistula has been observed only once at this Vascular Center. The patient (Case 8) sustained a perforating wound of the right popliteal space from a German pistol. He developed marked swelling of the popliteal space and severe ischemia of the leg and foot which resulted in extensive necrosis of the muscles and gangrene of the great toe. The characteristic thrill of an arteriovenous aneurysm was palpable in the popliteal region but in addition a pulsating tumor was also present. Since peripheral gangrene in association with an arteriovenous fistula is exceedingly rare, the possibility of a coexistent arterial aneurysm was considered. Preoperative measurement of the pressure by direct puncture of the aneurysmal sac revealed it to be 74 mm. of mercury, considerably higher than the initial pressure generally found in cases of arteriovenous fistulas. At operation a false aneurysm of the lower popliteal artery was encountered. After intrasaccular closure of the component vessels, an arteriovenous fistula was discovered which involved the artery two inches distal to the first aneurysm. After excision of this fistula adequate circulation was observed.

#### ARTERIOVENOUS FISTULAS

The pressure was measured within the arteries or aneurysms in eleven patients suffering from arteriovenous fistulas. The results are summarized in Table II. In the first case, in addition to the arteriovenous fistula, there was a large aneurysmal sac in the thigh.

**CASE 14 (Registry No. 2410)**—A 23 year-old sergeant was wounded in the right thigh by a shell fragment on Nov. 21, 1944. Approximately two weeks later a pulsating mass was discovered in the right thigh, and this increased in size for one week. A continuous thrill was palpable over this tumor and on auscultation there was a continuous bruit with systolic accentuation, indicating an arteriovenous aneurysm. An arteriogram, taken Feb. 9, 1945, showed a large aneurysm on the medial side of the right upper thigh with a fistula between the femoral artery and vein. After the collateral circulation had been sufficiently established he was operated upon June 23, 1945. The superficial femoral artery was exposed both above and below the aneurysm and these vessels were controlled by pieces of rubber tubing. A needle was then inserted into the aneurysmal sac and the pressure was found to be 35 mm. of mercury. Upon compression of the artery above the sac the pressure immediately fell to 12 mm. of mercury. Release of the compression allowed the pressure to rise to 35 mm. of mercury. When the distal artery was occluded, the pressure rose to 40 mm. of mercury, indicating that at least some of the blood coming down through the femoral artery was proceeding beyond the fistula into the arteries of the lower leg. In Fig. 5 are indicated the vascular findings.

The femoral artery was then dissected away from the aneurysmal sac and the opening into the latter closed by pressure while the laceration in the femoral artery, which measured 1.5 cm. in length, was closed with a continuous longitudinal suture of 000 black silk.

TABLE II. MEASUREMENTS OF PRESSURES IN ARTERIOVENOUS FISTULAS

CASE NUM- BER	HOS- PITAL REG- ISTRY NUM- BER	ARTERY IN- VOLVED	IN- ITAL PRES- SURE	OCCLU- SION OF PROX- IMAL ARTERY	OCCLU- SION OF DISTAL ARTERY	OCCLU- SION OF PROX- IMAL VEIN	OCCLU- SION OF DISTAL VEIN	OCCLU- SION OF PROX- IMAL ARTERY AND BOTH VEINS	TREAT- MENT	RESULT
13	9416	Superior femoris						72	Excision	
14	4210	Superior femoris	35	12	40				Long repair	Arteriogram P.O.
15	5415	External iliac						54	Excision	
16	4251	Profunda	46	30					Excision	Normal cir- culation
17	5504	Popliteal	30	22				86	Trans- verse repair	Arteriogram P.O.
18	4649	Superior femoris	70	10	72	80	70	46	Excision	Slight clau- dication
19	6842	Popliteal	35	0	30	56	38	10*	Trans- verse repair	Arteriogram P.O.
20	5876	Superior femoris	30	0	Throm- bosed	70	30		Excision	Normal cir- culation
21	5778	Carotid jugular	30	0	36	64	40	52	Trans- verse repair	Normal cir- culation
22	5611	Superior femoris						38	Excision	Normal cir- culation
23	2819	Common femoris	38	0	48				Excision	Slight clau- dication

\*Additional venous communication discovered after separation of fistula

on an atraumatic needle. After suture of the artery the rubber tubing was released and good pulsation was transmitted across the suture line. The aneurysm was then opened widely, clots evacuated, and the openings of the femoral vein into and out of the sac were closed with stitch ligatures. No attempt was made to excise the sac. After operation the patient made a good recovery and an arteriogram taken on July 27, 1945, demonstrated patency of the superficial femoral artery.

The second case represents the findings in a simple case of arteriovenous fistula in which the component arteries and veins were readily secured.

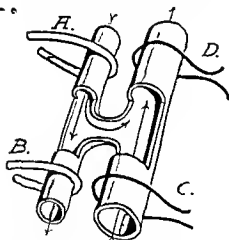
CASE 17 (Registry No. 5504)—A 21 year old soldier was wounded in the right popliteal space by a mortar fragment Dec 21, 1944. At the time of admission to this Vascular Center on March 23, 1945, he presented typical evidence of an arteriovenous fistula in the popliteal space. An arteriogram taken by injection of diodrast into the femoral artery on May 27, 1945, visualized the femoral artery well to the popliteal space and at this point there was considerable reflux of the opaque material into the popliteal vein. He was operated upon Aug 9, 1945, and after controlling the circulation through all the component vessels a needle was inserted into the aneurysmal sac and the pressures were measured. The initial pressure was 30 mm. of mercury. With compression of the proximal artery the pressure dropped to 22 mm. of mercury. When the proximal artery and both the component veins were occluded the pressure increased to 86 mm. of mercury, indicating a very abundant collateral circulation. The findings are shown in Fig 6.

With the vessels controlled the artery was dissected away from the vein and the communication was found to measure 1 cm. in diameter. The opening in the vein was closed with a longitudinal running stitch and the arterial laceration was closed transversely after

excising a wedged shaped section of the damaged arterial wall. After release of the constricting rubber tubing excellent circulation was observed across the line of suture and an arteriogram taken Aug. 24, 1945, demonstrated the patency of the popliteal artery.

In the third patient there was not only a fistula between the profunda femoris artery and vein with a large aneurysmal sac in the thigh, but in addition the collateral circulation was well developed with considerable supply of blood to the fistula by retrograde flow.

CASE 16 (Registry No. 4251)—A 39 year old soldier sustained a perforating machine gun wound of the upper thigh on Sept. 17, 1944, and developed a large arteriovenous aneurysm of the thigh. He was operated upon July 15, 1945, and the common femoral artery was exposed just below Poupart's ligament. A very large profunda femoris vessel was found coming from the posterolateral side of the artery and appeared to communicate with the aneurysm. Compression of this artery, although it reduced the bruit, did not completely abolish it. Dissection was then carried down the thigh to expose the superficial femoral artery at the lower part below the aneurysm. The needle was inserted into the aneurysm and the initial pressure was found to be 46 mm. of mercury. With compression of the profunda the pressure dropped to 30. This failure of the pressure to drop still

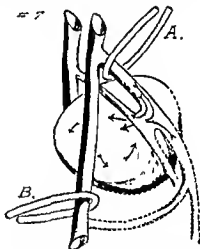


Popliteal Arteriovenous Aneurysm

Initial pressure = 30 mm. Hg.

Compression at A—22 mm. Hg. A + D + C = 6 = 22

Fig 6 (Case 17)—Diagram of circulation.



Arteriovenous Aneurysm profunda femoris

Initial pressure = 46 mm. Hg.

Compression A = 30 mm. Hg. A + B 18 mm. Hg.

Fig 7 (Case 16)—Diagram of circulation

further was interpreted as evidence that considerable collateral supply was entering the sac from below. Constriction of the distal femoral artery now caused the pressure within the sac to fall to 18 mm. of mercury. With the profunda femoris occluded above the aneurysm and the superficial femoral occluded below it, the sac was incised and the openings of the component arteries and veins were controlled by digital pressure until they could be closed with transfixion sutures. Fig 7 is a diagrammatic drawing of the operative findings. No attempt was made to excise the aneurysmal sac but it was drained through a stab wound on the side of the thigh. The postoperative course was uneventful.

*Comment.*—Intra-aneurysmal pressure studies in this case were useful in disclosing the presence of large collaterals which had to be secured before the sac could be opened safely.

Arteriovenous fistula between the carotid artery and the cavernous sinus has been observed only once in the series. It was interesting to note the drop in pressure from 110 to 50 with occlusion of the common carotid and a further fall to 44 mm. of mercury when the external carotid was also occluded. Because, in my experience, this pressure was close to the border line of pressure compatible with survival of the peripheral tissues, the external carotid artery was not ligated. Following ligation and division of the common carotid artery this patient had complete cessation of the bruit over the right temporal region for six weeks. A slight recurrence of the bruit was then noted. Exploration of the internal carotid three months later revealed that this artery was thrombosed at the site of the former ligation.

#### DISCUSSION

The blood pressure levels observed in the cases of arteriovenous fistulas are similar to those reported in the literature. The first reference to this subject was that of Bramann<sup>3</sup> in 1886, who observed a blood pressure varying between 56 and 64 mm. of mercury in a vein of the forearm proximal to an arteriovenous fistula of the brachial vessels. In 1908, von Oppel<sup>4</sup> used a tonometer on the digits and reported in detail the pressures observed in one case of arteriovenous aneurysm of the axillary vessels. The initial pressure was 40 mm. of mercury. With ligation of the proximal artery the pressure dropped to zero. The patient was then returned to the operating theater and the proximal vein was ligated. However, the pressure still remained at zero. Accordingly, the patient was returned to the operating room again and dissection was carried out behind the aneurysm to disclose the presence of a second vein through which the blood escaped from the aneurysm. After ligation of this vein the blood pressure returned to the initial level of 40 mm. of mercury. Korotkow, according to Coenen,<sup>2</sup> used the Riva-Rocci technique for the determination of blood pressure in cases of aneurysms and found that with pressures of 30 mm. of mercury the survival of the peripheral tissues was assured. However, in case the pressure dropped to zero, the outlook was unfavorable. Matas<sup>1</sup> reviewed the various tests and signs which are available for determining the efficiency of the collateral circulation at the time of operation, and commented that he was forced to abandon the blood pressure test even after repeated trials because of the difficulty of obtaining accurate measurements, especially in the lower extremities.

In experimental animals the blood pressure after the production of arteriovenous fistulas has been measured by the use of glass cannulas. Ney<sup>5</sup> in 1913 found in a typical experiment that the arterial pressure decreased from 131 to 80 mm. of mercury. Directly above the fistula the arterial pressure changed from 115 to 83 and the venous pressure increased to 72 mm. of mercury. Although the levels of pressure observed in these experiments are considerably higher than those observed in clinical cases, it is possible that the resistance

offered by the mechanical four-way glass cannulas was greater than that offered by the simple communication between the arteries and veins in these cases.

In studies which were carried on by Reid<sup>6</sup> to investigate the cause for the dilatation of the artery proximal to arteriovenous fistulas, the use of direct measurement of the blood pressure was suggested. The author stated, "Pressures obtained through a needle introduced into the lumen of the vessel seemed plausible and experiments to determine this point are now in progress." Further report in these experiments has not been found.

The dramatic fall of the pressure within the fistula, with ligation of the proximal artery, serves again to emphasize the disastrous consequences which follow this procedure. Matas has repeatedly called attention to the danger of proximal artery ligation and Makins<sup>7</sup> spoke of the high incidence of gangrene observed during the South African war following this procedure. Attention is called to the fact that a very misleading idea of the extent of development of collateral circulation is likely to be obtained from inspection of the distal extremity following temporary occlusion of the proximal artery in cases of arteriovenous fistulas. In one of the patients, after the artery proximal to the aneurysm had been temporarily occluded with a rubber tube, the endarteric appearance of the foot was so striking that excision of the fistula was deferred, on the basis that the patient did not have adequate collateral circulation. If either or both the component veins or the distal artery had also been occluded at the same time that the proximal artery was obstructed it is likely that the true character of the collateral circulation would have become evident.

The relatively low pressures observed in aneurysms associated with arteriovenous fistulas is again of significance from the standpoint of the occurrence of secondary hemorrhage. Although the occurrence of expanding hematoma or frank external hemorrhage is not unusual in cases of arterial aneurysms, the occurrence of these complications in arteriovenous fistulas is rare. In a previous communication<sup>1</sup> attention was called to this unusual complication and a case was cited in which the rupture occurred following application of an elastic pressure dressing. Since the pressure within the aneurysmal sac increases abruptly and considerably following obstruction of the venous outflow, as can be seen in Table I it is not surprising that rupture may be precipitated by the injudicious application of pressure to the tissues surrounding such an aneurysm. Again, thrombophlebitis of the component vein has been observed in three patients at the time of operation for arteriovenous fistulas. It seems possible that occlusion of the venous outflow by thrombophlebitis of the vein might precipitate rupture of an arteriovenous aneurysm, especially if its walls had not become firmly organized.

Pulsating exophthalmos due to a fistula between the internal carotid artery and the cavernous sinus was observed in only one case in this series. It was interesting to note the fall of pressure from 100 to 50 following temporary occlusion of the common carotid artery and a further fall to 44 mm of mercury when the external carotid artery was also obstructed. It is well known that hemiplegia is more frequent following ligation of the internal carotid artery than it is following that of the common carotid. The observa-



The forceps are then taped to the skin and excellent immobilization is obtained in all planes. However, it is usually advised that the patient's leg be restrained if he is comatose or that he be instructed to refrain from gross movements of the leg if he is cooperative. The needle is then disconnected and a glass adapter used to connect the needle to a two-bottle, open intravenous setup so that blood may be pumped in at any rate desired (Fig. 2).

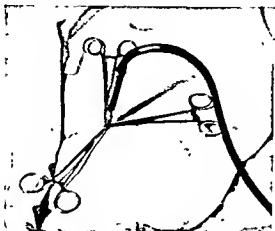


Fig. 1.—Close-up of inguinal region showing method of immobilization of the needle by the application of three forceps



Fig. 2.—Illustration of the entire two bottle, open infusion setup.

The leg is checked periodically for any swelling adjacent to the needle, but the intraluminal position of the needle can be checked at any time if a translucent solution is being infused by entirely occluding the rubber tubing about one foot from the needle with one hand while the tubing is pinched and released at a point between this level and the needle with position of the needle. This is always followed by an abundant influx of blood back into the glass adapter. In the cases of profound shock in which the femoral artery is used, a technique is used in which the No. 20 needle is inserted in a perpendicular plane at a point midway between the pubic tubercle and the anterior superior spine (point of maximum pulsation, if present) just below the inguinal ligament. A lighter colored blood pulsating rhythmically may force the plunger of the syringe back very rapidly but in cases of profound shock with associated anoxia only a small amount of dark blood may enter the syringe. As the arterial pressure gradually rises, the color of the blood lightens and pulsations increase such that raising the infusion set or increasing the pumping pressure becomes necessary. Simple withdrawal of the needle from the artery or vein and maintenance of pressure for a few seconds has not been followed by a discernible hematoma or concomitant difficulty in any case. The method has been used in five cases of profound shock in which no peripheral superficial veins were available, with gratifying results in each case, such as to encourage further use of the method.

#### SUMMARY

1 A method of efficient rapid transfusion is presented which is useful in cases in which multiple thrombosis or prolonged trauma to veins make ordinary venoclysis or venesection impossible.

2 The common femoral vein, a site just below the inguinal ligament, is used in those cases in which a good pulsation of the femoral artery is palpable.

3 In those cases in which the shock is of such a profound nature that the artery is not palpable, a concomitant collapse of the femoral vein occurs frequently enough so that the femoral artery is more practicable. The artery is conveniently located at the mid-point between the pubic tubercle and the anterior superior spine.

4. A method of immobilization of the needle is presented

5. Blood, plasma, or fluids can be dripped or pumped in under pressure at any desirable rate

6 Simple withdrawal of the needle from the artery or vein and maintenance of the pressure for a few seconds has not been followed by a discernible hematoma or concomitant difficulty in any case

7 It is hoped that the method may be more widely utilized in emergency situations in patients without an adequate superficial peripheral venous network.



The lowest mean arterial pressure found after excision of an aneurysm or arteriovenous fistula was 32 mm. of mercury. With pressures at or above this level, adequate circulation to the peripheral tissues has been observed in these patients.

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## A METHOD OF RAPID TRANSFUSION INTO THE FEMORAL VESSELS IN PATIENTS WITHOUT ADEQUATE PERIPHERAL SUPERFICIAL VEINS

J. ORDIE SHAFER, M.D., MINNEAPOLIS, MINN.

THE method described here is suggested as an efficient method of rapid transfusion in cases in which the usual venous route is impossible. In many cases of prolonged daily intravenous infusions in which the patient has been on parenteral feedings for weeks the veins of all the extremities are obliterated so that even when multiple venesections are done it is found that the superficial venous channels are unsuitable for infusions. These patients can then, of course, be given hypodermoclysis or proctoclysis if the oral route is not available for feeding, but should an emergency situation such as profound shock arise, plasma or blood is needed urgently and the patient may soon die if the blood volume is not replenished within a short time. The following method of femoral infusions has proved very effective and efficient at the University of Minnesota Hospital in these cases.

After having prepared the skin of the groin adjacent to the inguinal ligament with a suitable antiseptic solution, the area in the groin is palpated for the pulsation of the femoral artery. When a good arterial expansile pulsation is felt, the large common femoral vein just adjacent on the medial side is almost always open and is an excellent site for transfusions. In those cases in which the shock is of such a profound nature that the pulsation of the femoral artery is not perceptible, the adjacent femoral vein is frequently collapsed and a transfusion into the femoral artery is then used. In both cases a two and one-half inch, 20 gauge needle with a short, beveled point is used. In the case of the infusion into the common femoral vein the arterial pulsation is located at or just above the inguinal ligament and the finger tips are arranged in a parallel direction on the medial side of the artery below the inguinal ligament. The needle on a 10 or 20 c.c. syringe is entered through the skin at a point just medial to the artery holding the needle and syringe perpendicular to the surface of the leg. The needle is then slowly advanced until dark venous blood slowly appears in the syringe. The usual range of depth is 2 to 3½ cm. Drawing back the plunger of the syringe is usually not necessary, but may aid in some cases. Following this, 5 to 10 c.c. of blood are withdrawn, injected, and withdrawn to ascertain that the needle is satisfactorily placed within the lumen of the vein. This identical procedure is also used frequently in these cases to draw blood specimens for diagnostic tests. After having carefully determined that the position of the needle is satisfactory or having further inserted or withdrawn the needle 1 or 2 mm. for satisfaction, a small Kelly forceps is clamped (first notch) on the needle as close to the skin line as possible. This is followed by two other forceps, placing each closely on top of the other and placing each approximately 120 degrees away from the other as shown in the accompanying Fig. 1.

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The forceps are then taped to the skin and excellent immobilization is obtained in all planes. However, it is usually advised that the patient's leg be restrained if he is comatose or that he be instructed to refrain from gross movements of the leg if he is cooperative. The needle is then disconnected and a glass adapter used to connect the needle to a two-bottle, open intravenous setup so that blood may be pumped in at any rate desired (Fig. 2)

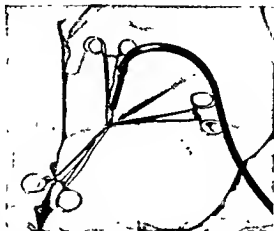


Fig. 1.—Close up of inguinal region showing method of immobilization of the needle by the application of three forceps

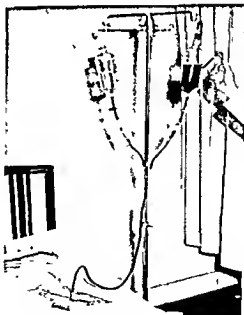


Fig. 2.—Illustration of the entire two-bottle open infusion setup

The leg is checked periodically for any swelling adjacent to the needle, but the intraluminal position of the needle can be checked at any time if a translucent solution is being infused by entirely occluding the rubber tubing about one foot from the needle with one hand while the tubing is pinched and released at a point between this level and the needle with position of the needle. This is always followed by an abundant influx of blood back into the glass adapter. In the cases of profound shock in which the femoral artery is used, a technique is used in which the No. 20 needle is inserted in a perpendicular plane at a point midway between the pubic tubercle and the anterior superior spine (point of maximum pulsation, if present) just below the inguinal ligament. A lighter colored blood pulsating rhythmically may force the plunger of the syringe back very rapidly but in cases of profound shock with associated anoxia only a small amount of dark blood may enter the syringe. As the arterial pressure gradually rises, the color of the blood lightens and pulsations increase such that raising the infusion set or increasing the pumping pressure becomes necessary. Simple withdrawal of the needle from the artery or vein and maintenance of pressure for a few seconds has not been followed by a discernible hematoma or concomitant difficulty in any case. The method has been used in five cases of profound shock in which no peripheral superficial veins were available, with gratifying results in each case, such as to encourage further use of the method.

#### SUMMARY

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5 Blood, plasma, or fluids can be dripped or pumped in under pressure at any desirable rate.

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7 It is hoped that the method may be more widely utilized in emergency situations in patients without an adequate superficial peripheral venous network.

## WOUND HEALING STUDIES ON SEVERAL SUBSTANCES RECOMMENDED FOR THE TREATMENT OF BURNS

BROCK E. BRUSH, M.D., CONRAD R. LAM, M.D., AND JOSEPH L. PONKA, M.D.  
DETROIT, MICH.

*(From the Division of General Surgery of the Henry Ford Hospital)*

SEVERAL years ago, a study of the methods of treatment of burns in several large industrial plants revealed that almost a hundred different ointments, powders, and solutions were being used.<sup>1</sup> Almost none of these substances had been subjected to critical investigation with regard to their effect on wound healing. Recently there has been a trend toward simplification and standardization in local burn therapy. Tannic acid is no longer used and the shortcomings of sulfonamide ointments and many other preparations have been recognized. However, the number of substances which are being advertised and sold as burn remedies is still too large. Several of these which are being used or were formerly used have been chosen for controlled studies. This report also presents the results of tests of some experimental ointments which were undertaken at the request of the Subcommittee on Burns and Surgical Infections of the Committee on Medical Research.

The following substances were tested: tannic acid solution, tannic acid in tragacanth jelly, commercial tannic acid jelly (Ameritan), petrolatum gauze, two kinds of carbowax ointment, mineral oil and aluminum monostearate preparation, proflavine dihydrochloride, Biodyne ointment, and Hydrosulphosol solution.

The experimental method was that previously employed by two of us in investigating the effect of a number of agents on the healing of cutaneous wounds.<sup>2</sup> This procedure was essentially that of Carrel and Hartman.<sup>3</sup> Usually, each substance was tested on twelve guinea pigs. Under ether anesthesia, the abdomen was shaved, prepared with an antiseptic solution (hexyl-chloro-meresol) and two circular cutaneous defects were made, one being on each side of the midline. The wound on the animal's left was used as the test wound and the other served as a control. The wounds were approximately the same size and were usually about the size of a dime (Fig. 1). The defects were outlined on sterile cellophane to record the size, after which the material to be tested was placed on the appropriate wound. Sterile gauze dressings were placed on each wound and held with adhesive tape which passed entirely around the animal's body. The dressings were changed every two days until both wounds were healed. At each dressing, tracings of the wound areas were made and more of the test substance was applied. The cellophane tracings were transferred to white paper for a permanent record (Fig. 2).

Part of the work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Henry Ford Hospital.

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A typical experiment on twelve animals is represented by the results obtained by the application of 5 per cent tannic acid solution (Table I). It is seen that in no instance did the wound treated with the test solution do better than the control, and in eight of the ten animals who survived, there was delay in healing of the treated side. From this, it is concluded that the solution is inhibitory to wound healing and in the summary column in Table III, this effect is indicated.



Fig 1—Freshly made cutout wounds on the abdominal wall of the guinea pig, the experimental substance will be applied to the wound on the animal's left.

#### NO. 3

Date	3/3	3/5	3/7	3/9	3/11	3/13	3/15
Left	○	○	○	○	○	•	H
Right	○	○	○	○	•	H	H

Fig 2—Tracings showing rate of healing in a typical experiment. Hydrosulphosol was applied to the wound on the left at each dressing. Note that the control wound healed first.

A second typical experiment is illustrated in Table II. In eight, or two-thirds, of the animals treated by the application of hydrosulphosol solution, at least one more dressing was necessary on the treated side and it is concluded that the material is moderately inhibitory.

#### COMMENT ON THE SUBSTANCES TESTED

Since the use of tannic acid in burns has fallen into disrepute because of the toxic effect on the liver and the demonstration by several investigators that there is inhibition of wound healing,<sup>4,6</sup> it might seem unnecessary to give this method further consideration. Actually, however, the experiments on tannic acid in tragacanth jelly were carried out in May, 1941, at a time when the coagulation method of treatment was being used extensively. The subsequent tests were made to confirm the growing suspicion regarding tannic acid and to show the value of this simple pilot type of experiment. Since twenty-five of the twenty-eight treated wounds showed delay in healing, it is impossible to escape

the conclusion that tannic acid is detrimental to wounds. If this experiment had been done years ago, it probably would have led to an earlier careful scrutiny of the tanning method (Fig 3).

Petrolatum gauze has been used extensively as a dressing for burns, granulating surfaces, and skin graft donor sites. It has been generally assumed that it is an inert type of dressing. Often, it is spoken of as a control treatment as compared with a presumably active substance. In these experiments, petrolatum

TABLE I. FIVE PER CENT TANNIC ACID SOLUTION  
(DAYS REQUIRED FOR HEALING)

ANIMAL NUMBER	CONTROL WOUND (DAYS)	TEST WOUND (DAYS)	HEALING
1	15	19	Delayed
2	Expired third day		-----
3	13	23	Delayed
4	11	19	Delayed
5	15	21	Delayed
6	19	21	Delayed
7	13	15	Delayed
8	15	21	Delayed
9	11	11	No effect
10	11	21	Delayed
11	15	15	No effect
12	Died eighth day		

Summary Delay in eight of ten animals which survived, cause of death in two animals not known

TABLE II. HYDROSULPHOSOL SOLUTION  
(DAYS REQUIRED FOR HEALING)

ANIMAL NUMBER	CONTROL WOUND (DAYS)	TEST WOUND (DAYS)	HEALING
1	10	14	Delayed
2	10	12	Delayed
3	10	12	Delayed
4	12	12	No effect
5	10	12	Delayed
6	12	12	No effect
7	12	14	Delayed
8	10	12	Delayed
9	12	12	No effect
10	8	10	Delayed
11	10	12	Delayed
12	12	12	No effect

Summary Delay in wound healing in eight of twelve animals

TABLE III. SHOWING NUMBER OF ANIMALS IN WHICH HEALING WAS HASTENED, UNAFFECTED, OR DELAYED, WITH CONCLUSIONS AS TO EFFECT OF TEST SUBSTANCE

SUBSTANCE TESTED	HASTENED	NO EFFECT	DELAYED	CONCLUSIONS
Tannic acid solution (5% aqueous)	0	2	8	Delayed
Tannic acid jelly (tragacanth)	0	0	6	Delayed
Tannic acid jelly (Amertan)	0	1	11	Delayed
Petrolatum gauze	1	7	2	No effect
Carbowax ointment A	2	4	6	Delayed (f)
Carbowax ointment B	1	5	5	Delayed (f)
Stearate grease	2	5	2	No effect
Proflavine dihydrochloride	0	5	7	Delayed
Hydrosulphosol solution	0	4	8	Delayed
Biodrene ointment	2	4	6	Delayed (f)

gauze was compared with a dry gauze dressing. It appeared to have no effect on the time necessary for the healing of these small wounds.

During World War II, the Subcommittee on Burns and Surgical Infections of the Committee on Medical Research interested itself in a search for better ointment bases to be used as vehicles for the sulfonamides and penicillin and for use as bland dressings or for gauze impregnation. At the request of the committee, we carried out some tests on a carbowax base in two combinations. That referred to in Table III as carbowax A had the following composition: carbowax\* 4000, 21 Gm., propylene glycol,\* 64.5 Gm., methyl cellulose (25 cps) 2.5 Gm., Vodol O 1<sup>†</sup> (lecithin) 0.25 Gm., and mineral oil, 12 c.c. To this mixture was added 12 per cent of a lipophilic base consisting of aluminum monostearate-mineral oil base containing Tween 60.

Each type of carbowax ointment tested showed slight delay in wound healing in one-half of the animals.



Fig. 3—Delay in healing from the use of tannic acid jelly, the control wound on the animal's right is healed.

Another experimental ointment which was studied was that referred to in Table III as stearate grease. This was a mixture of mineral oil and aluminum monostearate. The wounds dressed with this healed in the same time as the controls. In a series of twelve animals, stearate grease was applied to one wound and carbowax A to the other. In one-half of these, the side with stearate grease healed first, in four the rate of healing was the same, and in two the side with carbowax healed first, indicating a slight advantage for the grease.

During the war, there was a revival of interest in a group of local antiseptics known as aminoacridine compounds or flavines. This was particularly true in Great Britain. One group<sup>†</sup> advised the use of proflavine sulfate for granulating areas and burns. Other investigators\* showed that a 1:1000 solution of proflavine buffered to a pH of 6.2 was harmless when applied to the rabbit's exposed

\*The carbowax and propylene glycol were obtained by the committee from the Union Carbide and Carbon Company. Carbowax B was an ointment prepared by the Rysan Company and was said to consist of carbowax 4000, carbowax 1500, glyceryl monostearate, propylene glycol, and distilled water.



brain tissue. (In the same experiment, acriflavine in that concentration produced tissue damage.) Proflavine dihydrochloride\* was applied to the test wound in twelve of our animals. The control wound healed first in seven animals, indicating a slightly inhibitory effect of the test solution.

From time to time, there has been interest in the role of sulfur in wound healing. In 1930, Reimann published a paper entitled "Use and Reasons for the Use of Thioeresol to Stimulate Wound Healing."<sup>9</sup> In this article he stated, "The naturally occurring chemical radical -SH which stimulates mitosis has been discovered. Advantage is taken of the chemical group sulphhydryl to stimulate the healing of wounds." It is notable that neither of the two wounds described in the communication were entirely healed at the time of the report. Further favorable comment followed.<sup>10</sup> Then there were several papers<sup>11-13</sup> recommending the use of a proprietary preparation, hydrosulphosol, which contains the -SH radical (sulphydryl). A critical review of these three papers leaves one unconvinced that the solution actually had a beneficial effect on the burns. Tissue culture studies by Salle and Korzenovsky<sup>14</sup> showed that chicken heart cultures in contact with the material failed to grow unless the hydrosulphosol was diluted 1:80. With seventy-two hours contact, it was necessary for the dilution to be increased to 1:400 before there was growth of the culture.

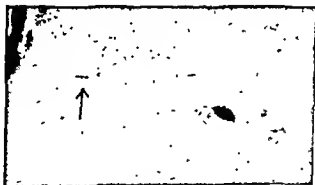


Fig 4.—Delay in wound healing with the use of hydrosulphosol, the control wound (arrow) is healed.

When hydrosulphosol was tested on the guinea pig wounds, there was delay in healing in two-thirds of the animals (Table II and Fig 4). In no instance did the treated side heal before the control side. The conclusion was that the material was moderately inhibitory to wound healing.

About three years ago, several lay publications contained some accounts of a preparation known as biodyne ointment, and it was alleged that there was remarkable rapidity of healing when the substance was applied to burns.<sup>15, 16</sup> Shortly afterward, Hirschfeld, Pilling, and Maun<sup>17</sup> tested biodyne on dermatome graft donor sites on human beings and experimental animals. The control wounds were covered with petrolatum gauze. They found no evidence that

\*Manufactured by Mallinckrodt Chemical Works, St. Louis, Mo.

biodyne accelerated the healing process. Current advertising states that the ointment embodies the property of "acceleration of rate of healing and epithelization."

In our experiments, the control wound was healed before the wound treated with biodyne in one-half of the series. Twice the treated wound healed first; in the remaining four animals both wounds healed on the same day.

#### SUMMARY

A number of substances which have been suggested or recommended for the treatment of burns have been applied locally to small wounds in guinea pigs and the healing time compared with that of control wounds in the same animal which were treated with dry gauze. Tannic acid in solution and in jellies caused a marked delay in healing. Proflavine dihydrochloride (1:1000) and hydrosulphosol were moderately inhibitory. Biodyne ointment and two kinds of carbowax base gave slight delay in one-half the animals. Wounds dressed with petrolatum gauze and a stearate grease healed in the same time as the controls.

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## THE TREATMENT OF BEDSORES IN PARAPLEGIC PATIENTS

MAJOR BROMLEY S. FREEMAN, MEDICAL CORPS, ARMY OF THE  
UNITED STATES

(From the Section on Plastic Surgery of the Hines Memorial Hospital, Hines, Ill.)

UNTIL very recently the active surgical treatment of bedsores, especially those in paralyzed patients, not only has been neglected but condemned. Munro<sup>1</sup> in an excellent résumé of the care of spinal cord injuries published in 1940 advised against any form of surgical interference. The literature is replete with injunctions regarding the prevention of bedsores, with multiple recipes for salves, ointments, and local applications, a myriad of beds including sawdust, water, air mattress, as well as plaster casts, frames, and suspension apparatus have been advocated. Except for Davis<sup>2</sup> who advised the replacement of atrophic scars resulting from bedsores by means of plastic procedures thus giving padding to bony prominences, no advocate for the surgical treatment of the ulcerated lesion had come forth until reports of the treatment of paraplegic patients in World War II were announced.<sup>3,4</sup>

As one of the centers for treatment of spinal cord injuries requiring the group consultation of neurosurgeon, urologist, physical therapist, orthopedist and plastic surgeon, we were confronted with approximately 200 ulcers in approximately fifty patients. Traditional passive therapy was continued until, in an otherwise healthy patient, a large ulcer exposing the entire sacrum caused a secondary osteomyelitis and finally a *Bacillus proteus* septicemia. Although massive penicillin therapy was instituted immediately and surgical attempts to control the infection were made, the patient died. At this point a critical survey of the spontaneous healing and the results of our passive treatment pointed to the necessity for a more dynamic approach.

Lewis<sup>4</sup> has shown that ischemia of six to twelve hours damages the skin; continuous ischemia for twenty-four to forty-eight hours or frequently shorter periods results in necrosis of the skin. Relief of ischemia, if not prolonged, is followed by a reactive hyperemia which flushes out the injurious metabolites and restores the tissue if the relief interval is long enough. Moreover, Lewis and others have shown that in normal individuals a pressure of 50 to 60 mm. of mercury is sufficient to arrest the blood flow in the skin. In the normal individual muscular tone and firm subcutaneous tissue interpose a padding between the arterial supply and the pressure points, permitting a more diffuse spread of pressure. Removal of these interposing factors would permit a viselike obliteration of the vessels between the skeleton and the point of pressure. Lessening of the padding between the nonresistant hard surface and the bony prominence through disuse atrophy, as well as by alteration of the skin and tissues by hypoproteinemia, causes a tighter tourniquet around an area of skin, augments the

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constricting pressure, and obliterates the local circulation. In paraplegic patients lessening of the padding between the skin and the bone, not only by disuse atrophy but through the loss of subcutaneous fat due to general debility, alteration of the elasticity of the tissue by absence of muscular tone, and hypoproteinemic edema, reduces the normal buffering effect, and pressure is placed directly upon the local blood vessels permitting arrest of the blood flow and ischemia. Moreover, the disuse of the legs and hips results in a decreased blood supply to this area, resulting in atrophy of tissue and an obvious impairment in healing.

Experimentally, however, local reflex tests of the circulation on all of our patients showed good results with histamine and scratch. Compared with normal skin above the line of the cord lesion the lower extremities showed an equal timed response to the histamine flare and wheel as well as the tache test, giving evidence of good local circulation. Except for the reduction of the blood supply and the anesthesia in these paralyzed individuals, we found no contraindications for operating other than those found in sympathectomized limbs. In the treatment of severely injured extremities and in postirradiation defects, we had noted the improved circulation developed by rotating, tubed, or pedicle flaps and felt that, with a minimum of trauma, surgical closure of these defects could be carried out.

Clinically, three types of onset of the decubitus ulcers have been noted in the group of patients under study. The first and most common after slight trauma in well-nourished individuals showed a purplish discoloration of the skin followed by swelling, a gradual change in color to normal, and later a small central necrotic area. A second type usually seen after prolonged trauma in well-nourished individuals had its onset in vesiculation followed by epidermal necrosis, leaving nonhealing, shallow ulcerations with piled up hyperkeratotic borders, which showed no change for periods of months. The third type found in debilitated patients showed immediate blanching, followed by massive necrosis and slough invading deeply into the tissue spaces. Repeated insult or infection will permit the formation of the usual extensive, undermining advancing ulcer.

The majority of patients received their initial bedsores in some period before or during evacuation while they lay for hours without turning. However, despite the most exacting nursing care we have observed bedsores arise almost spontaneously in patients who are debilitated markedly and show a depleted protein level. Unless their protein level is kept very high, the slightest trauma, overmassage, or too intensive local heliotherapy can result in ulceration. The average patient under our care had lost from 20 to 30 pounds, had no appetite, and their already depleted protein reserves were gradually draining from ulcerations. As anorexia was common and high protein, high caloric diets of little value unless they were ingested, recourse was made to intravenous protein hydrolysates, plasma, and blood as well as interval oral amino acids. As shown by Mulholland,<sup>7</sup> many ulcers healed spontaneously and most of them diminished markedly in size as soon as the negative nitrogen balance was compensated. Extra vitamins were given with emphasis on vitamins B and C.

and the time-honored preprandial insulin, 5 to 10 units, was given to those with intractable anorexia resulting in a rather marked improvement in appetite and a consequent rise in body weight and serum protein. As the blood supply of the surrounding area appeared inadequate for the disposal of dead tissue, sloughs were removed surgically. Local dressings of tyrothricin on fine mesh gauze were allowed to dry in place and mechanic's waste used for pressure dressings. Many of the ulcers, especially those around the groin, were exposed to the air for prolonged periods to permit drying. At no time were continuous wet dressings, which macerate the skin, or ointments used. The tendency of the ulcers to undermine and form deep extensive sacculations between tissue spaces was most frequent over the sacrum and trochanters. In several cases the lining of the sac was attached to the periosteum and almost completely encircled the bone. These were mechanically cleaned with irrigations of hydrogen peroxide and saline and packed with tyrothricin-impregnated fine mesh gauze. It was found impracticable to attempt sterilization of the ulcer, and clinical evidence of clean margins and absence of signs of inflammation were used to determine the appropriate time for surgery. Nonetheless, bacteriologic studies of many of the ulcers were made to be certain that any specific therapy could be instituted at once. Elevated temperature, urinary sepsis, and gross infection were the only contraindications to operation. Emaciated patients were prepared by multiple transfusions, plasma infusions, and other intravenous medications. These patients despite a very high protein intake showed evidence of a negative nitrogen balance because of the marked loss through drainage from the dressings, and it was thought advisable to institute surgery as soon as feasible.

The choice of the type of surgical intervention was dependent upon the individual case. Split-thickness skin grafts (.012 to .018 inch) were used to cover extensive sacral ulcers draining large amounts of protein in debilitated patients as a temporary expedient. Skin grafts were also used to close superficial epidermal necroses over well-padded areas. Several hyperkeratotic lesions on the buttock were similarly excised and grafted.

Penetrating ulcers forming saclike projections vastly larger than the external orifice were carefully dissected en bloc. The excision was carried out by sharp dissection without entering into the grossly contaminated sac. Any break in technique called for discarding the contaminated instrument or glove. In several cases the bare bone was exposed and every attempt was made to remove the sac lining completely, though the temptation was very great to curette the surface and leave the bone covering intact. Although microscopic examinations of the lining revealed epithelialization for only a few centimeters or less directly under the external opening, it was felt that the blood supply was insufficient to cope with even the slightest amount of contaminated tissue left behind, and the entire scar tissue was removed.

The closure of the external defect was dependent upon the position of the lesion, the laxity of the tissue, and the presence of other bedsores. Direct primary approximation was carried out only when layers of fascia could easily be brought together to take tension off the skin and wide undermining permitted easy closure without tension. This was possible only in lesions of the anterior-

superior spine area and the small but deeply invasive gluteal ulcers. Larger gluteal ulcerations and smaller trochanteric lesions were closed by advancement flaps or swinging flaps with marked undermining and careful approximation of the subcutaneous layers. Thick rotation flaps either singly or double were used for closure of the larger defects over the trochanters, the sacrum, and the ischial spines. Marked undermining usually lessened the original defect and in the majority of cases the donor site could be closed by primary suture. However, when any evidence of tension presented, the donor site was closed with a thick split-thickness graft.

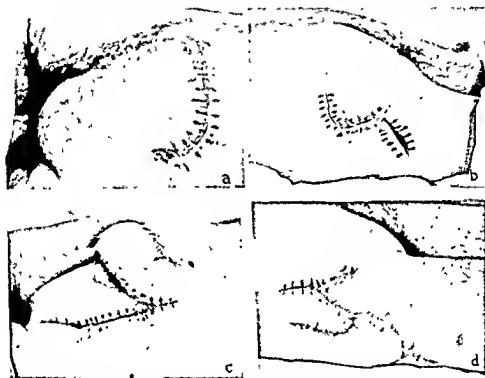


Fig. 1—Types of repairs after excision of necr. ulcer, and deep extensions. a, Defect (5 by 7 cm.) of right gluteal region repaired by wide undermining and simple advancement flap. b, Two rotation flaps in form of Z-plasty used to close defect after excision of trochanteric ulcer with adherent peritosteal extension (shown in Fig. 2). c, Transposition flap from right gluteal region closing 8 by 10 cm. sacral defect. d, Extensive trochanteric lesion closed by rotation flaps from thigh and gluteal region.

Technically, meticulous care was used in handling the flaps to avoid undue trauma. Fine tissue hooks were used throughout; mosquito clamps and hot packs were used for hemostasis and only the finest cotton sutures for ties and closure. In the earlier cases sulfadiazine was dusted into the wound, but later a solution of penicillin was instilled after hemostasis was completed, the wound irrigated, and the sutures ready for tying. After a few seromas in the larger wounds it became a practice to insert a thin half-tube drain through a stab wound to aid the removal of serum and blood upon the application of a large pressure.

dressings of mechanic's waste held in place by elastoplast adhesive or elastic bandage. This drain was removed in twenty-four hours. Replacement of blood loss was carried out by transfusion during or immediately after the operation. Penicillin was administered twenty-four hours prior to the operation and continued systematically for seven to ten days when the sutures were removed and collodion or adhesive bridges used to support the edges. Turning was carried out at three-hour intervals but the operative sites, although well padded with mechanic's waste pressure dressings, were spared. As shown by the examples in Fig. 1, allowing the skin sutures to remain for any period over a week resulted in crosshatching and scarring. Nonetheless, because of the tendency toward delayed tissue repair and the possibility of wound separation, it was thought advisable to forego cosmetic perfection and tend toward a stable wound.



Fig 2—Trochanteric ulcer with periosteal extension dissected out en bloc. Note small external opening and large deep extension which surrounded the greater trochanter (see Fig 1, b)

Immediately after hearing of the excellent work of Gibbon and Freeman,<sup>9</sup> a few multiple rotating flap operations entailing a dissection of the entire lumbar sacral and upper gluteal region were done, but the vast extent of the dissection and the blood loss in already debilitated patients persuaded us to return to single rotating flaps. Croce's<sup>8</sup> operation, similar in extent, also entails a midline scar directly over the lumbar and sacral spines which it is felt will be subject to later trauma. In some of the better nourished patients who have thin adherent scars, excision of the sacral and trochanteric areas have been carried out and flaps used for replacement as suggested by Davis.<sup>8</sup> After fourteen days light massage was given under the direct supervision of the surgeon to loosen the wound, mobilize the scar, and increase the local nutrition. At no time was heliotherapy administered locally.



Fig. 3—Rotation flap method of closing sacral defect. a, Improvement in patient's nutrition sufficient to permit partial scar closure of sacral ulcer deep extension is not visualized in photograph. b, Lin bloc excision of scar, ulcer, and extension down to sacral periosteum in midline. c, Left Gluteal flap raised and adjacent area undermined at fascial level. d, Flap transposed and defects closed. sufficient laxity resulted from undermining to permit right-sided plastic closure.



In only three out of fifty cases were there recurrences of bedsores. Two patients with well-healed flaps over the ischial tuberosities insisted upon sitting through dinner and a long show lasting eight hours with resultant ulcerations directly over the flap. A third patient with a healed thick skin graft over the sacrum blatantly refused either to eat or to get off his back. The constant pressure, plus urinary sepsis, permitted the skin graft to vanish in less than two weeks. A review of these three patients revealed that in the first two the protein levels, although high after preliminary treatment, had been allowed to fall from 8 and 7.6 mg, respectively, to 6.3 and 5.7 milligrams. The third patient's protein level had never gone above 5.8 mg and was definitely on the downgrade. A checkup on the rest of the operative patients showed an increase in protein level rather than a decrease, and, although several others had attended the dinner and a show for so prolonged a period, only those two with a diminished protein level had a recurrence. The operative procedures are prolonged and tedious, but the results obtained, the improvement of general health, and the restoration of ambulation in wheel chair, crutches, or braces, as well as the frequent discharge of these patients to their homes without the need of constant dressings and drainage, have paid dividends. We no longer watch, over a period of six months or a year, for the slow spontaneous healing of ulcers which result in tissue-paper thin scars easily traumatized.

The youth and excellent health of the patients prior to injury have tremendously influenced our results, but a dynamic approach to the problem of bedsores even in the aged should show returns in longevity and general improvement. It must be emphasized, however, that this regime could not have been carried out without the cooperation of an interested and aggressive urologist<sup>10</sup> and an indefatigable staff of nurses and dietitians.

#### SUMMARY

A review of 200 bedsores in fifty paraplegic patients revealed that simple operative procedures could be carried out successfully to close the defects if plasma protein levels were raised to and maintained at normal.

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gall bladder is even greater than the figures indicate. One can say with some assurance that in the presence of a temperature over 102° F and white blood count over 15,000 there is at least an even chance that one will find a severe acute cholecystitis and often actual gangrene. However, the converse of this statement is not necessarily true, for in a previous study in this hospital, Tourroff<sup>2</sup> has shown that many acutely inflamed gall bladders, especially when subsiding, will have few or no clinical manifestations.

*Operation.*—In general, so-called early operation was performed on these patients. Early operation is an indefinite term, used here to mean operation within one to three days after admission. Since the majority of patients had been ill for an additional one to three days prior to admission, it follows that operation was performed in from two to six days after the onset of the illness. Many were operated upon the first hospital day, there being only enough delay to confirm the diagnosis and prepare the patient adequately for surgery. In a few cases, operation was delayed several days to a week or more, usually because the diagnosis was not certain and conservative therapy was deemed wiser.

Of the 109 patients subjected to operation, ninety-six had a cholecystectomy and thirteen a cholecystostomy. Cholecystostomy was done only in severely ill and aged patients. Five of these patients were jaundiced, two had perforations of the gall bladder with a bile peritonitis, two others had gangrenous gall bladders, and the remainder were acutely ill with associated degenerative diseases. In this group of thirteen patients there were two deaths. One of these occurred in a 67-year-old patient with diabetes who had a perforated gall bladder with peritonitis, and who developed a hemiplegia three days postoperatively; the other was in a 68-year-old woman with marked jaundice, in poor general condition, who died on the operating table. This high mortality is indicative of the extremely serious condition of these patients, rather than the danger of the operative procedure. It is occasionally stated that cholecystostomy has as high or higher mortality than cholecystectomy but cholecystostomy is done only on the poor-risk patients, on whom any operative procedure will produce a high mortality.

Of the eleven patients who survived after cholecystostomy, one had a partial cholecystectomy by sloughing portions of a gangrenous gall bladder following operation, two returned within one year for cholecystectomy, the remaining eight patients have remained well to date. This observation is in accord with Elliason and Stevens,<sup>3</sup> who reported that following cholecystostomy for acute cholecystitis, 84 per cent of patients remained well. While cholecystostomy is not the procedure of choice for acute cholecystitis, it has definite indications and is often followed by good results.

Cholecystectomy was performed in ninety-six patients in this series. Drainage to Morison's pouch was used routinely in all cases. In seven of these cases a choledochostomy was performed. Five of these patients who were jaundiced will be considered separately. In the remaining two patients who were not icteric, the ducts were dilated, one caused by a palpable stone, and in the other nothing was found to account for the dilatation. In this group of ninety-six



cases in which the stones are not impacted or the occasional case of noncalculous gangrenous cholecystitis. In this connection, Colp and Doubilet<sup>7</sup> and others<sup>8, 10</sup> have drawn attention to the clinical significance of pancreatic reflux. They have reported cases of acute noncalculous cholecystitis which were probably due to the necrotizing effect of an activated pancreatic reflux.

*Jaundice.*—The clinical significance of jaundice in acute cholecystitis was one of the prime objects of this study. In reviewing the cases it was not always easy to decide just what constituted jaundice. In those cases in which there was a definite discoloration in the skin and mucous membranes, laboratory results were usually confirmatory and there was no question as to the jaundice. However, some patients had an increase in icterus index, without bile in the urine, whereas others had detectable bilirubin in the urine, without an elevated icterus index. It was found that a number of patients showed the transient presence of bilirubin in the urine one or two days postoperatively, with prompt disappearance thereafter. Therefore, the criterion which was established for jaundice was an icterus index of 10 or more, together with bilirubin in the urine, and with or without visible icterus in the skin and mucous membranes. In this way, six patients who had icterus indices ranging from 10 to 15, but without bile pigment in the urine, were omitted from consideration, and two with bile in the urine on a single determination but no elevation of icterus index or clinical jaundice were also omitted. It was felt that possible errors in laboratory work would be overcome by these standards.

Nineteen patients in this series fulfilled the criterion of jaundice at the time of operation. This was an incidence of 17 per cent. Six of these patients, or approximately one-third, had a previous history of jaundice, and the remainder were jaundiced for the first time. The ages of the patients varied from 32 to 72 years, with a mean of 56, which is somewhat higher than the average for acute cholecystitis in general. The duration of dyspepsia or colic prior to the attack for which the patient was admitted was very variable and there was no apparent correlation between duration of symptoms and jaundice. However, the majority of the patients had had symptoms for less than four years.

A comparison was made between the clinical and laboratory findings in these jaundiced patients with those found in the group as a whole.

TABLE III

	NUMBER OF PATIENTS	PALPABLE GALL BLADDER	PER CENT OF PALPABLE GALL BLADDER	PALPABLE LIVER	PER CENT OF PALPABLE LIVER
Jaundiced	19	9	47	6	31
Nonjaundiced	90	19	19	17	19

Reference to Table III shows that palpable gall bladders were present in almost one-half the jaundiced patients, and more than twice as frequently as in the nonjaundiced. Similarly, the ratio of palpable livers was 31 to 19 per cent, respectively.

There was no significant characteristic to the temperature or white count. Eleven of the patients had a temperature of less than 102° F., and eight were

over 102° F. Thirteen had white blood counts of less than 15,000 and six were over 15,000.

Liver function tests were done in two-thirds of the cases. These were either cephalin flocculation or cholesteryl esters, or both. In one-half the cases in which these tests were done, the laboratory results indicated liver damage. Liver function determinations are notorious in their fluctuation and difficulty of interpretation. A certain number of "normal" individuals in the older age group will show an abnormal response to these tests. Therefore, the findings in this series must be considered as suggestive of liver damage, rather than conclusive. Even if actual liver damage is present in any case, it is not certain that this is due to an hepatitis. The existence of hepatitis and cholestasis is postulated by numerous writers.<sup>11-13</sup> However, this relationship has been questioned by Culp and associates,<sup>14</sup> who found that when biopsies were aspirated from the liver depths and subjected to careful histologic study, the liver cells showed no changes in cases of cholelithiasis without jaundice. In cases with jaundice, there was a focal liver cell degeneration, which represents a reaction to bile stasis rather than a direct relation to the primary disease in the gall bladder. It would seem, therefore, that when liver damage is present in a patient with cholelithiasis, it is a secondary effect of obstruction rather than a direct accompaniment of the gall bladder disease.

Of the nineteen jaundiced patients, thirteen had a cholecystectomy and six had a cholecystostomy. Only three of the nineteen had cancerous gall bladders, which is a somewhat lower incidence than for the group as a whole. This would seem to indicate that jaundice is not necessarily associated with a severely inflamed gall bladder.

The common bile duct was enlarged in six cases and normal in the remaining thirteen. The dilated ducts were explored. Stones were found in five patients. In two of these no stones were palpable, but a choledochotomy was instituted because of the dilatation and jaundice, and small stones were found. Such incidents prove that palpation alone cannot be used as an index to the presence of stones.

Of these six jaundiced patients who had explorations of the common duct, one died with liver abscesses and septicemia evidently due to a suppurative cholangitis, one other patient in whom a cholecystostomy had been done continued to have colic. Bilepercutum was performed within two years, a cholecystectomy was done for chronic cholelithiasis, and stones were again removed from the common duct. Thereafter, he did very well. The remaining four patients in this group made a good recovery and have remained well.

There were thirteen jaundiced patients in whom the common bile duct was not explored. The follow-up on these thirteen patients showed that five made excellent recoveries with an uneventful course thereafter. Three had fairly good results, with mild dyspeptic symptoms, two patients were lost to the follow-up clinic, one was an operative death previously mentioned. It is noteworthy that of the ten patients in this group who were followed, all obtained relief from the jaundice without exploration of the common duct. Only two patients had

recurrence of colic and jaundice within one and one-half years, and they were reoperated upon and the common ducts explored. In one of these patients, stones were found in the common duct and removed. In the other, the common duct was enlarged, but no stones were present. Both of these patients made an excellent recovery and have remained well since operation.

From these cases one can deduce that jaundice plus dilatation of the common duct demands exploration of the duct, since stones were found in five out of six such instances. However, jaundice, alone, in the presence of a normal common duct, is not an absolute indication. These patients are relieved of their jaundice following simple removal (or sometimes only drainage) of the gall bladder. In a small proportion (two out of ten) one can expect recurrence of jaundice and the necessity of a secondary operation. However, in the majority of cases they will remain symptom-free. Unfortunately, it cannot be predicted, at the time of the initial exploration, in which group the patients will fall, and it becomes a matter of judgment in deciding upon the procedure. In those cases in which the jaundice subsequently disappears without choledochotomy, one may ascribe the jaundice to small, nonpalpable stones which were passed spontaneously, to inflammatory edema around the duct which subsided, or to spasm of the sphincter mechanism incident to the acute cholecystitis.

*Follow-up*—Among the 109 patients in this series, there was a total of four postoperative deaths, or a mortality of less than 4 per cent. The remaining 105 patients were followed for a period of one to six years. Adequate follow-ups were obtained in eighty-five cases, and in twenty there was no adequate follow-up. The results of treatment were arbitrarily divided into three groups—very good, fairly good, and poor. Seventy patients had very good results, meaning that they were symptom-free. Nine patients had fairly good results, signifying relief of pain, but persistence of some indigestion. In six cases the results were classed as poor, because of persistence of pain as well as indigestion. There were only three cases of noncalculus cholecystitis in this series, and among these the follow-up disclosed a poor result in one patient and a fair result in another. This is too small a group from which to draw conclusions. However, it has been observed repeatedly that patients undergoing cholecystectomy for noncalculus cholecystitis are especially prone to certain postoperative complaints which constitute the "post-cholecystectomy syndrome."<sup>14</sup> Some of these symptoms may have been due to a primary dyskinesia of the sphincter mechanism,<sup>15</sup> and, therefore, the removal of the gall bladder did not eradicate the major pathology, hence the higher incidence of postcholecystectomy symptoms in cases of noncalculus cholecystitis.

#### SUMMARY

1. In a study of 109 cases of acute cholecystitis, there was frequent correlation between the severity of inflammatory process in the gall bladder and the temperature and white count. Where the temperature was over 102° F. and the white blood count was over 15,000, the gall bladder was gangrenous in at least one-half the cases.



2. Cholecystectomy is the procedure of choice for acute cholecystitis, but even when cholecystostomy was done, the majority of patients remained symptom-free without any further surgery.

3. Stones were found in 97 per cent of acute cholecystitis.

4. Of the acutely inflamed gall bladders, 20 per cent were gangrenous. Gangrenous gall bladders had higher incidence (59 per cent as compared to 28 per cent) of positive bile cultures than nongangrenous, but the proportion of *B. coli* organisms was approximately the same (69 per cent versus 63 per cent). *B. coli* may be a secondary invader in the lumen of an inflamed gall bladder.

5. Gangrene of the gall bladder in some cases is due to obstruction of the cystic duct by stone, causing increased tension within the lumen, and interference with venous return. Noncalculus gangrene may be due to the necrotizing effect of an activated pancreatic reflux.

6. Of the acute cholecystitis cases, 17 per cent of the patients were jaundiced. The gall bladder and liver were enlarged more frequently in these cases than in simple acute cholecystitis. However, there was no conclusive evidence that hepatitis was a constant accompaniment of cholecystitis.

7. Jaundice plus a dilated common duct demands exploration of the duct because stones were usually found, even if not felt. However, jaundice without duct dilatation disappeared after simple operation on the gall bladder. In only two out of ten cases was there recurrence of jaundice necessitating a secondary operation. Only one of these patients had stones in the common duct, the other having an enlarged duct without stones.

8. Persistence of dyspepsia after cholecystectomy may be due to a dyskinesia of the sphincter mechanism.

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## INTRATHECAL PENICILLIN IN BACTERIAL MENINGITIS

ROBERT G. LIVINGSTONE, M.D., BOSTON, MASS., AND

JOHN E. LEFACH, M.D., NEW YORK, N. Y.

(From the Head and Neck Department and the Department of Medicine of the Memorial Hospital, New York, N. Y.)

REPORTED experiences with the intrathecal administration of penicillin in bacterial meningitis are currently of considerable interest. Thus used penicillin has given promise of acting in many instances as a reasonably safe and effective therapeutic agent, but nevertheless by this route it has also led in certain cases to failures and to complications of such nature that the tentative recommendations usually made for its administration have not been generally accepted. A successful experience with penicillin administered intrathecally in large doses in bacterial meningitis prompts the following reports and comments.

### CLINICAL REPORTS

Streptococcal meningitis developed as an acute postoperative complication in two patients recently subjected to radical surgical procedures on the head and neck service of the Memorial Hospital.

A clinical diagnosis of meningitis was made first in one patient on the eighth day following excision of recurrent carcinoma within the nasal cavity. Confirmatory evidence was afforded when cerebrospinal fluid obtained by lumbar puncture was shown to contain *Streptococcus viridans* in pure culture. Treatment by orally given sulfonamides and by intramuscularly administered penicillin in the usually recommended doses was immediately instituted. Clinical response was prompt and striking, but because of recurrent positive cerebrospinal fluid cultures direct instillation of penicillin into the subarachnoid space seemed indicated. By lumbar puncture, five daily doses of 100,000 units of sodium penicillin dissolved in 5 c.c. of cerebrospinal fluid were administered intrathecally. No untoward effects, with the possible exception of generalized convulsions of undetermined origin following the fourth and fifth injections, were observed. The patient was discharged home as cured fourteen days after the institution of intrathecally administered penicillin.

A more extensive procedure, involving excision of the right maxilla and exenteration of the right orbit, was associated in the other patient with inadvertent puncture into the subarachnoid space. A gauze pack moistened with penicillin solution was applied to the wound, and treatment by whole blood transfusion, intravenously given sulfonamides, and intramuscularly administered penicillin was ordered. By the third postoperative day unmistakable clinical signs of meningeal infection developed. Lumbar puncture was promptly performed, and turbid cerebrospinal fluid which clotted readily was obtained under an abnormally elevated pressure. Through the same needle 50,000 units of

sodium penicillin freshly dissolved in 5 c.c. of normal saline solution was at once instilled into the subarachnoid space. Initial cultures yielded a pure growth of *Streptococcus hemolyticus* (group A). Clinical response again was prompt, and after one week of uneventful daily treatment by this route the intrathecal administration of penicillin was discontinued. The patient has since then remained essentially well.

More detailed information concerning these patients is presented in the accompanying case reports.

#### CASE REPORTS

**CASE 1.**—The patient was a white woman 59 years of age who was admitted to the hospital on Dec. 19, 1943, because of recurrent epidermoid carcinoma within the nasal cavity. Almost two years previously the cartilaginous part of the lower two thirds of the nose had been excised, the nasal septum and a large portion of the upper plate of the hard palate had been removed, and the anteromedial half of the right maxilla had been resected. Wide excision of the area of recurrent disease was carried out under intravenous sodium pentothal anesthesia on Dec. 21, 1943. During this procedure the cribriform plate of the ethmoid bone was exposed, and curettage of the ethmoid and sphenoid sinuses was performed. A gauze pack moistened with sodium penicillin solution was applied to the surface of the wound.

The immediate postoperative course (Fig. 1) was uneventful until a severe frontal headache developed on the evening of the third day. The following morning the patient was found moaning and thrashing about violently in bed, completely disoriented and uncooperative. The temperature was 102° F., and the blood pressure was 160/70. The wound margins were reddened, and both malar areas were slightly edematous. There was no nuchal rigidity. All abdominal reflexes, except for a transient reaction in the right upper quadrant, were absent. The deep tendon reflexes were hyperactive but equal bilaterally. An equivocal right Babinski response was obtained. Roentgenographic examination of the chest showed no relevant abnormalities.

A tentative diagnosis of encephalitis, attributed to retrograde extension of septic thrombosis from the operative site, was made. Sulfathiazole was given by mouth in an initial dose of 2 Gm. and a maintenance dose of 1 Gm. every four hours, and sodium penicillin was given intramuscularly in doses of 30,000 units every three hours. Within a few hours the patient was cooperative and well oriented, but she continued to complain of persistent frontal headache. The fever slowly subsided, and sulfadiazine was given in place of sulfathiazole.

On the seventh day the temperature rose to 103° F., and the blood pressure was found to be 220/120. No localizing neurologic signs were present. Lumbar puncture was performed, and clear, colorless fluid under a pressure of 250 mm. of water was obtained. There was no evidence of lumbar block. Quantitative cell counts were not obtained, but microscopic examination of the uncentrifuged fluid showed 22 polymorphonuclear cells per high power field. A differential white blood cell count showed 90 per cent polymorphonuclear cells, 3 per cent monocytes, and 7 per cent small lymphocytes. The temperature twenty-four hours later was 101° F., and the blood pressure was 180/70. Slight nuchal rigidity was present, and a positive Kernig's sign was found. There was a Babinski response on the right side. A second lumbar puncture was performed, and slightly cloudy fluid under a pressure of 300 mm. of water was obtained. Cultures of the previously withdrawn fluid showed a pure, heavy growth of *Str. viridans*. The dose of sodium penicillin was increased to 80,000 units every four hours.

The signs of meningeal irritation largely disappeared by the ninth day. The temperature was 99.6° F., and the blood pressure was 118/80. A number of transfusions of whole blood were given, and continued improvement was noted clinically in the ensuing seven days. The differential white blood cell count at the end of this time showed 83 per cent



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superior, medial, and lateral walls of the right antrum was demonstrable on roentgenographic examination. Tissue obtained by excision biopsy of the nasal portion of the tumor showed epidermoid carcinoma.

Radical removal of the tumor, involving excision of the right maxilla and exenteration of the right orbit, was carried out under intravenous sodium pentothal anesthesia on Feb. 15, 1946. During this procedure inadvertent entry into the subarachnoid space occurred, and cerebrospinal fluid was at once observed to be escaping freely from the puncture site. A gauze pack moistened with sodium penicillin solution was immediately applied to the area. Sodium sulfadiazine was given intravenously in doses of 25 Gm twice daily, and sodium penicillin was administered intramuscularly in doses of 20,000 units every three hours.

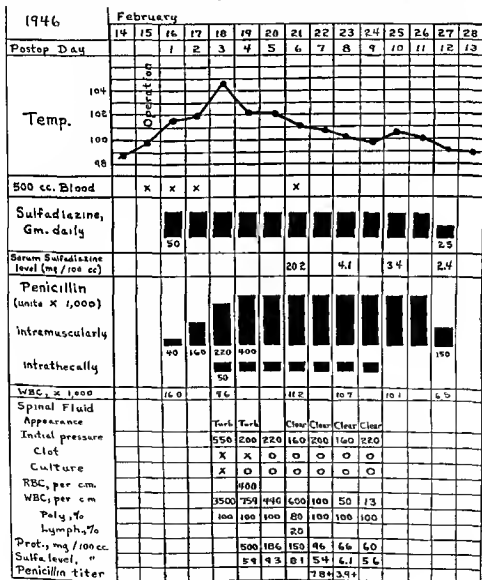


Fig. 2 (Case 2).—Hospital course, Feb. 14 to 23, 1946

Cultures from the ethmoid and sphenoid sinuses at this time showed heavy growths of *Str viridans* and scattered colonies of nonhemolytic *Staphylococcus aureus*, *Aerobacter aerogenes*, and nonhemolytic gamma *Streptococcus*.

The necessity for more aggressive treatment became apparent as clinical improvement failed to occur. Cultures of cerebrospinal fluid taken on the nineteenth, twentieth, twenty-second, and twenty-fourth days were reported as positive on the twenty-fourth, twenty-sixth, twenty-sixth, and twenty-seventh days, respectively. On the twenty-seventh day a freshly made solution of 100,000 units of sodium penicillin in 5 c.c. of cerebrospinal fluid was slowly injected into the subarachnoid space, and when no immediate ill effect was noted a series of similar daily injections by this route was instituted.

About seven hours after the fourth intrathecal injection of penicillin the patient suddenly cried out loudly and exhibited two generalized convulsions which together lasted one or two minutes. She bit her tongue and frothed slightly at the mouth. Her eyes were turned up and to the right. The pupils were round, regular, and equal. No localizing neurologic signs were found. In five minutes or less a period of somnolence supervened. The patient could be roused, but she was unable to speak. A few hours later she seemed to be her usual self, though she had no recollection of the convulsive episode.

This complication was attributed to the prolonged course of the meningitis rather than to the possibly toxic effect of the therapeutic agent. A fifth intrathecal injection of penicillin was administered on the following morning. About seven hours later the patient began to complain of fatigue and of dull frontal headache. Within a short time she was found curled up in bed with the sheets drawn over her head, convulsions but drowsy and transiently disoriented. There was some cyanosis of the face and hands. Mild photophobia was noted. The left arm was held stiffly outstretched for one or two minutes. The pupils were dilated but round and equal. There was slight bilateral papilledema. The deep tendon reflexes were hyperactive and equal bilaterally. The blood pressure was 160/80. No specific treatment was given.

On the following day there were no abnormal physical signs. The patient, however, was confused and disoriented in all spheres. She was quiet and cooperative, and she accepted food and medication without comment. Lumbar puncture yielded clear, colorless fluid under normal pressure and sterile on culture. As a provocative measure a dose of 10,000 units of sodium penicillin dissolved in 5 c.c. of cerebrospinal fluid was administered intrathecally. No untoward reactions were observed throughout the ensuing forty-eight hours.

Now considerably improved and well oriented the patient recalled her period of "forgetfulness" during the several preceding days. Temperature remained within normal limits. The white blood cell differential count showed 79 per cent polymorphonuclear cells, 2 per cent eosinophilic cells, and 16 per cent small lymphocytes. A second dose of 10,000 units of sodium penicillin was given intrathecally, and then all medication, including the sulfonamides and all intramuscularly administered penicillin, was arbitrarily discontinued.

Cultures of the sphenoid sinuses taken at this time showed *Monilia albicans*, *A. aerogenes*, *Staph aureus*, nonhemolytic gamma *Streptococcus*, and *Str viridans*. A small gauze pack moistened with isotonic saline solution was kept over the wound surface. No evidence of recurrent meningeal infection was noted. On the thirty-seventh day the patient was permitted to sit up and within twenty-four hours she was out of bed and completely asymptomatic. Finally, on the forty-first postoperative day, fourteen days after the institution of intrathecally administered penicillin, she was discharged home as cured.

The patient was last seen on March 21, 1946. She was engaged in her normal pursuits, and she appeared to be in excellent health.

CASE 2.—The patient was a white woman 58 years of age, who was admitted to the hospital on Feb. 11, 1946, with a tumor of the right maxillary antrum of about four months' duration. Diplopia had been present for two or three days. Physical examination on entry showed slight ptosis of the right eye, slight swelling of the right cheek and right peri-orbital tissues, and an obstructing tumor in the right nasal cavity. Bone destruction of the

infecting organisms in the cerebrospinal fluid. A heavy growth of *Str. viridans* was obtained within twenty-four hours from a specimen withdrawn by lumbar puncture at the end of this time. No assay of the penicillin concentration in the cerebrospinal fluid was attempted, however, and no determination of the sensitivity of the infecting organisms to penicillin was made. The administration of 300,000 units of sodium penicillin over an uninterrupted period of forty-eight hours to the second patient likewise failed to exert an appreciable effect on the organisms in the cerebrospinal fluid. Cultures of a specimen withdrawn when the first lumbar puncture was performed yielded a heavy growth of *Str. hemolyticus* (group A). As subsequent study later showed, the strain of infecting organism here encountered was relatively resistant to penicillin. An adequate concentration of the intramuscularly administered penicillin had apparently never been attained in the cerebrospinal fluid.

Given intravenously in bacterial meningitis, penicillin has not definitely been shown to have appeared in appreciable concentrations in the cerebrospinal fluid.<sup>11</sup> Single injections of various doses have been administered empirically to patients, but the reported results,<sup>10, 11</sup> while admittedly successful, have included no substantiating laboratory data.

More information is available concerning the concentrations of intravenously given penicillin in the absence of acute meningeal infection.<sup>9, 11, 12</sup> Significant levels in the cerebrospinal fluid, demonstrably effective against the commonly encountered infecting organisms, have not been attained with doses of ordinary magnitude, but titers approaching therapeutic requirements have been noted when doses of 10 to 25 million units,<sup>12</sup> administered over a twenty-four period by the intravenous drip technique, were utilized to breach the "hemato-encephalic barrier."<sup>9</sup> The possible relationships between the total dose and the various body fluid concentrations thus suggested require further investigation.

Localized thrombophlebitis, more recently averted to some degree by recourse to the concurrent administration of heparin, has been reported as a hazard of the intravenous route,<sup>1, 6</sup> and systemic evidence of toxicity, manifested by nausea and vomiting or by the development of azotemia, has been mentioned as a consequence of massive dosage.<sup>13</sup>

Direct instillation of penicillin into the subarachnoid space in the absence of lumbar or ventricular block assures effective concentrations throughout the cerebrospinal fluid. The obvious advantage provided by this route of administration is reflected in the many successfully treated cases of bacterial meningitis which have been recorded.<sup>2, 4, 9, 12, 17, 19</sup> Laboratory control, except initially in fulminating cases, is highly desirable to permit individualization of the general plan of treatment, and daily penicillin administration, utilizing a small volume of cerebrospinal fluid or sterile normal saline solution as the solvent, is probably best continued until satisfactory clinical response is evident and persistently negative cultures are obtained. Concurrent treatment with sulfonamides and intramuscularly administered penicillin is recommended to suppress the intensity of extrameningeal infection.<sup>8, 17, 19</sup> The possible acquisition of resistance to penicillin by the infecting organisms encountered, associated if it occurs with a corresponding decrease in virulence, need occasion no immediate concern.



The immediate postoperative course (Fig. 2) was uneventful. On the third day the patient became noticeably quiet and unresponsive. A sudden chill occurred, and the temperature rose abruptly to almost 105° F. Examination then showed moderate nuchal rigidity and hyporeflexive, but bilaterally equal, deep tendon reflexes. The left retinal field was normal in appearance. There were no localizing neurologic signs. Lumbar puncture was performed, and turbid cerebrospinal fluid which readily formed a colloidlike clot was obtained under a pressure of 550 mm. of water. Through the same needle 50,000 units of sodium penicillin freshly dissolved in 5 c.c. of normal saline solution were slowly injected into the subarachnoid space. No untoward reactions were noted. The dose of intrathecally administered penicillin was at the same time increased to 50,000 units every three hours.

The next day the patient was much improved, and the nuchal rigidity was appreciably diminished. Cultures of the previously withdrawn cerebrospinal fluid showed a pure, heavy growth of *Str. hemolyticus* (group A). A second dose of 50,000 units of sodium penicillin was administered intrathecally, and a series of daily injections by this route was instituted. On the seventh day estimation by a serial dilution method of the penicillin level in the cerebrospinal fluid twenty-four hours after the previous therapeutic administration by this route showed a concentration of 7.8 units per cubic centimeter. The infecting strain of *Str. hemolyticus* (group A) was found to be inhibited by a concentration of 3.2 units per cubic centimeter but unaffected by a concentration of 1.6 units per cubic centimeter. On the following day similar examination of the cerebrospinal fluid showed a level of 3.9 units of penicillin. A specimen of blood serum obtained at the same time, three hours after the preceding intrathecal injection, was found to contain 0.1 unit of penicillin per cubic centimeter.

When clinical improvement seemed assured and when no further positive cerebrospinal fluid cultures had been obtained for six days, the intrathecal administration of penicillin was discontinued. No evidence of persistent or recurrent meningeal infection was noted in the ensuing three days. Treatment with sulfonamides given intravenously and with penicillin administered intramuscularly was then also discontinued. The patient remained symptom free, and on the twenty-eighth hospital day, twenty-one days after the institution of intrathecally administered penicillin, she was discharged home as well.

#### COMMENTS

Recourse to the intrathecal administration of penicillin in large doses to patients with bacterial meningitis presupposes careful consideration of the more commonly accepted methods by which effective, harmless concentrations of this therapeutic agent might be achieved and maintained in the cerebrospinal fluid.

Given intramuscularly in meningitis, penicillin, with all credit to earlier efforts in this direction, is not known to have been consistently demonstrated in the cerebrospinal fluid in concentrations adequate to inhibit strains of some of the pathogenic organisms which have been encountered<sup>1,2,11</sup>. Successful treatment of bacterial meningitis with penicillin administered by this route, alone or in conjunction with orally or parenterally given sulfonamides, has been reported,<sup>10,12</sup> but evidence clearly supporting a definitive bacteriostatic action within the cerebrospinal fluid, rather than a more direct effect against a concurrent bacteremia or extrameningeal focus of infection, has not yet been offered.

The levels attained by the intramuscular route with doses considerably in excess of those usually recommended proved conspicuously ineffective in the patients reported here. The intramuscular administration of 8,640,000 units of sodium penicillin over an uninterrupted period of twenty-one days to the patient with *Str. viridans* meningitis failed to exert a noticeably adverse effect on the

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Explanation elsewhere is probably required for the sporadic failures which have been described in the treatment thus outlined.<sup>9</sup>

Administration of penicillin by this route is not without its dangers and uncertainties. Many serious complications, transient or persistent in nature, have been attributed to this treatment.<sup>9, 10-12</sup> Meticulous care in choosing preparations of penicillin intended for intrathecal administration is requisite, and stringent precautions to prevent the various secondary infections which are known to have occurred is mandatory. The risk of repeated lumbar punctures in the presence of presumably elevated intracranial pressure must always be considered.<sup>11</sup> Only by achieving and maintaining harmless, as well as effective, penicillin levels may the objections to this treatment of bacterial meningitis be for the most part disregarded.<sup>10</sup>

The timely administration of penicillin intrathecally to the two patients reported here probably led to their prompt recovery. No apparent advantage was gained by utilizing doses in excess of those required to attain an effective cerebrospinal fluid level, but no known sequel occurred to warrant subsequent arbitrary limitation of any clinically indicated dosage. The occurrence here of generalized convulsions during the course of treatment of the first patient might justifiably be attributed to chronic central nervous system irritation by the disease alone. Recourse to a similar plan of treatment in the care of future patients under comparable circumstances thereby seems justified.

#### SUMMARY

Penicillin administered intrathecally in large daily doses led to the prompt, essentially uneventful recovery of two patients with postoperative bacterial meningitis, one of whom did not respond to an adequate trial of parenteral penicillin and sulfonamide therapy.

Penicillin administered intrathecally in the absence of lumbar block is recommended as a very satisfactory therapeutic agent in the treatment of fulminating or sulfonamide-resistant bacterial meningitis.

Grateful acknowledgment is made to Dr. William S. MacComb for permission to report these cases.

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*Physiologic Considerations*—In consideration of the mode of administration and dosage of penicillin an important factor is whether the infection is primarily a generalized infection without abscesses (septicemia) or a local area of suppuration (abscess) that is relatively avascular. In a generalized infection without associated abscesses the effective bacteriostatic level of penicillin required in the serum as determined by the penicillin sensitivity of the infecting organism is the determining factor, whereas the permeability of the wall of the cavity to the penetration of the penicillin is the more important factor in a local lesion. Thus in a septicemia, the penicillin can be given by the usual intramuscular or intravenous routes of administration in variable dosages dependent upon the sensitivity of the causative organism. In a local lesion the permeability of the wall may be so reduced that even a very high concentration of penicillin in the serum remains ineffectual, and hence the mode of administration must be altered so that a higher penicillin concentration can be obtained locally. The more usual methods of administration of antibacterial drugs such as the oral, intramuscular, and intravenous routes are markedly less effective because of the dilution by the entire body fluids, and, second, because of both the local tissue barriers and vascular impairment in many of these cases. Topical application has proved somewhat effective superficially on wound surfaces but does not attain the penetration of the sites possible by the local or direct use as in the case of intrathecal, intra articular, or intramedullary (bone) administration. Thus, in the case of an early acute empyema, penicillin given within the pleural cavity may bring about a good therapeutic result, whereas the usual modes of administration are ineffectual even though a high bacteriostatic level in the serum is present. The appropriate method of administration therefore depends upon whether the sensitivity of the infecting organism to penicillin or the permeability of the wall of the cavity is the more important. However, in the extremities of the body, many cases present involvement of a wide area, and the penicillin penetration becomes a problem either because of the impaired blood supply or the presence of infection within fascial or bony pockets. Intramuscular or intravenous administration is frequently ineffectual, and local administration becomes impractical both because of the large area involved and because of the presence of multiple small compartments. In this type of case the intra-arterial administration of penicillin has proved very effectual. When the penicillin is injected intra arterially dilution remains minimal and the blood pressure forces the concentrated drug into the local area supplied by the artery. The distribution is further aided by the increased capillary permeability present in areas of local inflammation which permits a greater filtration of the agent locally.

The success of the arterial route was impressively shown, in a case reported by Fritzsche,<sup>10</sup> during therapy of a patient with generalized tetanus. Prior to therapy, the convulsions had been bilateral, but after one injection of serum into the left carotid, the convulsions almost disappeared on the right side but diminished very little on the left. This dramatically demonstrated the high concentration of medication possible in the distribution of an artery injected.

## INTRA-ARTERIAL PENICILLIN IN THE SURGICAL TREATMENT OF INFECTIONS OF THE EXTREMITIES

J. ORDIE SHAFER, M D, MINNEAPOLIS, MINN.

PENICILLIN has provided us with an effective antibiotic agent for the therapy of infections of the extremities. Unfortunately the problems of fibrous or osseous barriers and vascular impairment have frequently made high local concentration of penicillin unobtainable when given by the usual intramuscular or intravenous routes and the maximum beneficial effects hence have not been attained. Now, however, it has become possible to overcome some of these obstacles by the intra arterial administration of penicillin. This method effectively overcomes the factors of tissue barriers and vascular impairment and facilitates a greater control of acute and chronic infections of the extremities.

*Intra-arterial Therapy Discussion*—Intra arterial administration of various drugs has been used since 1914 to obtain a high local concentration of the desirable therapeutic agent in the tissues supplied by the artery. In that year Heddaus<sup>1</sup> injected antitetanic serum via the carotid route seeking a maximum concentration of this serum in the cerebral tissues. Goyanes<sup>2</sup> injected the arteries of the extremities with a cyanate solution attempting to secure a high local concentration within tuberculous joints. Fiolle and Fiolle<sup>3</sup> injected hydrogen peroxide intra-arterially in dogs while investigating the possibilities of parenteral oxygenation. The results obtained by these men were not remarkable but they introduced this useful method of obtaining a high local concentration within the tissues. Subsequently, Dos Santos,<sup>4,5</sup> Lamas,<sup>6</sup> De Fourmestraux,<sup>7</sup> Fredet,<sup>8</sup> Leriche,<sup>9</sup> Fritzsehe,<sup>10</sup> Demel and Sgalitzer,<sup>11</sup> and Luccarelli<sup>12</sup> have utilized mercurochrome, colloidal silver, acriflavine, metaphen, gentian violet, and various other medicaments and serums. With the recent advent of more effective chemotherapeutic agents, Martinoff<sup>13</sup> employed prophylactically sulfanilamide and mercurochrome intra-arterially in extremity wounds with success. A and E Titelbaum,<sup>14</sup> Russian surgeons, reported a series of fifteen cases in which 100 to 150 cc of 85 per cent sulfanilamide were used intra arterially with excellent results. E. Branco Ribeiro<sup>15</sup> injected sulfanilamide intra-arterially for infections of the extremities and was the first to record the use of intra-arterial penicillin injections. In 1944 he stated, "Because our experience with intra-arterial sulfanilamide has been adequately long we are authorized to state that this method considerably diminishes the period of treatment in relation to other methods and it is to be expected that the same will happen with intra-arterial penicillin." Recently, Glasser and his associates<sup>16</sup> in this country have given penicillin intra-arterially, using the technique of Dos Santos,<sup>5</sup> in which a blood pressure cuff placed proximally on the extremity is inflated to a pressure of 280 mm of mercury immediately following the injection and maintained at this pressure for ten minutes.

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The comparative efficacy of the various intra-arterial methods and the intravenous method of injection were demonstrated by injecting radioactive phosphorus by various techniques and determining the concentration at various sites on the extremity by the Geiger counter\*. Ambulatory patients with normal extremities were used to aid in ruling out the variability of circulatory impairment. In Table I are listed the ages and weights of the subjects used.

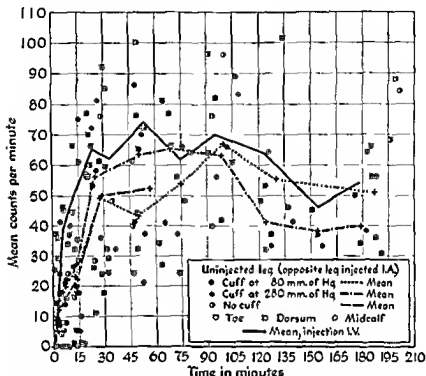


Fig 1—Radioactive phosphorus present in un.injected legs using the three different techniques of intra arterial injection

Four-tenths millicuries of radioactive phosphorus ( $P^{32}$ ) in 10 c.c. of normal saline solution were injected intravenously, intra-arterially into the femoral artery without accompanying stasis by cuff, with the cuff at a subdiastolic pressure (80), and at a supradiastolic pressure (280) following the injection at a rate of 1 c.c. per second. These studies as illustrated by Figs 1 to 5 revealed that all values taken by the intra-arterial method on the injected leg are over the mean for the intravenous method for a period of three hours, indicating that the intra-arterial method gives a higher local concentration in the leg than the intravenous method for this time. The maximum values obtained with the intra-arterial injection and the use of a blood pressure cuff for stasis remained over

\*I am indebted to the members of the Radiation Therapy Department of the University of Minnesota Hospital, K. W. Stenstrom, J. P. Marvin, and R. Plank for their cooperation during the investigation with radioactive phosphorus and to the Physics Department of the Massachusetts Institute of Technology for having supplied the radioactive phosphorus.

The application of a tourniquet proximally to obstruct the venous return materially aids the increased local concentration of the drug. Thus, Goyanes<sup>2</sup> was able to obtain anesthesia of an extremity after injection of procaine intra-arterially only when he applied a proximal tourniquet after injection. When the tourniquet was not applied no anesthesia was obtained, and occasional toxic effects of the drug were observed indicating a return of a large portion of the drug into the general circulation. Dos Santos<sup>4</sup> demonstrated in arteriographic studies that the injection of sodium iodide into the brachial artery with a tourniquet applied proximally revealed the arterial shadow to be visible for fifteen minutes. Then "as the vessel loses its opacity, the tissues gradually become more accentuated, obviously due to the fixation of sodium iodide in the tissues."

In the present series of cases a new method of treatment has been introduced in that the blood pressure cuff is inflated to a subdiastolic blood pressure before the injection of the penicillin. This effectively prevents the return of venous blood and at the same time the continued arterial pressure aids in the distribution of the penicillin into the tissues without significantly increasing the dilution of the drug. With this technique a complete subsidence of inflammatory edema has usually occurred within twenty-four to forty-eight hours. Important in this regard is the finding of Lewis and Grant<sup>11</sup> that an increase in the arterial amplitude of their plethysmographic tracings occurred during the period of congestion produced by venous occlusion. More important, however, they noted a reactive hyperemia with an increase in arterial flow up to 600 per cent following the release of venous congestion after a period of compression at 80 mm of mercury for fifteen minutes. Lewis<sup>12</sup> had also shown that the minute capillaries of the skin are able to contract against internal pressures of from 50 to 60 mm of mercury. However, since petechial hemorrhages may appear if the venous pressure is raised to 90 to 100 mm of mercury, the cuff is never inflated above 80 mm of mercury in intra-arterial injections and in congested or ulcerated legs a value of 60 mm of mercury is preferred.

Pumping the cuff to a high level above the systolic blood pressure following the injection is less efficacious since the benefits of venous hyperemia on the collateral circulation are not obtained and the propulsive force of the systolic pressure is lost.

TABLE I—LISTING OF AGES AND WEIGHTS OF PATIENTS USED FOR THE DETERMINATIONS

METHOD	PATIENT	AGE (IN YR.)	WEIGHT (IN LB.)
Intravenous	H. B.	33	98
	J. C.	68	137
Intra-arterial Cuff at 80 mm Hg	J. Z.	56	145
	J. O.	63	130
	O. T.	47	195
Cuff at 230 mm Hg	M. L.	30	111
	H. S.	70	125
	F. P.	72	160
No cuff	T. F.	72	139
	J. B.	67	127

The comparative efficacy of the various intra-arterial methods and the intravenous method of injection were demonstrated by injecting radioactive phosphorus by various techniques and determining the concentration at various sites on the extremity by the Geiger counter\*. Ambulatory patients with normal extremities were used to aid in ruling out the variability of circulatory impairment. In Table I are listed the ages and weights of the subjects used.

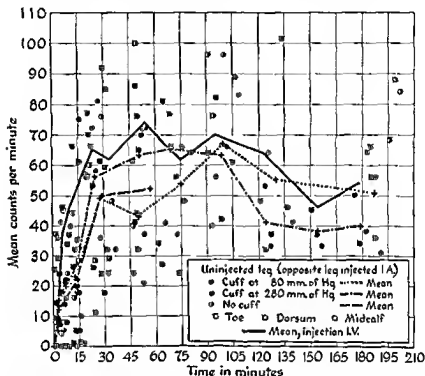


Fig. 1.—Radioactive phosphorus present in uninjected legs using the three different techniques of intra-arterial injection

Four-tenths millicuries of radioactive phosphorus ( $P^{32}$ ) in 10 c.c. of normal saline solution were injected intravenously, intra-arterially into the femoral artery without accompanying stasis by cuff, with the cuff at a subdiastolic pressure (80), and at a supradiastolic pressure (280) following the injection at a rate of 1 c.c. per second. These studies as illustrated by Figs. 1 to 5 revealed that all values taken by the intra-arterial method on the injected leg are over the mean for the intravenous method for a period of three hours, indicating that the intra-arterial method gives a higher local concentration in the leg than the intravenous method for this time. The maximum values obtained with the intra-arterial injection and the use of a blood pressure cuff for stasis remained over

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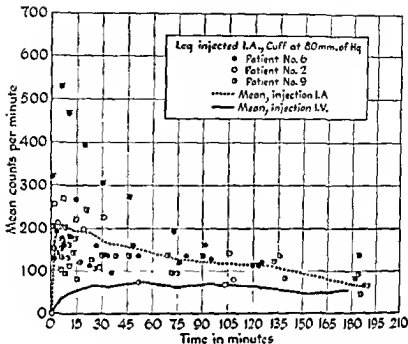


Fig. 2—Radioactive phosphorus present in legs injected intra-arterially with blood pressure cuff at 80 mm. of Hg.

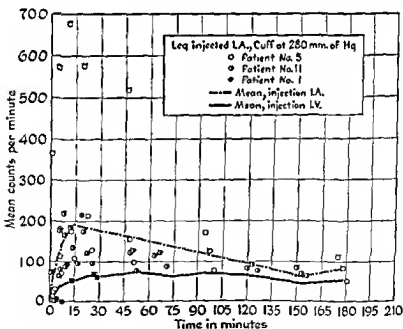


Fig. 3—Radioactive phosphorus present in legs injected intra-arterially with blood pressure cuff at 280 mm. of Hg.

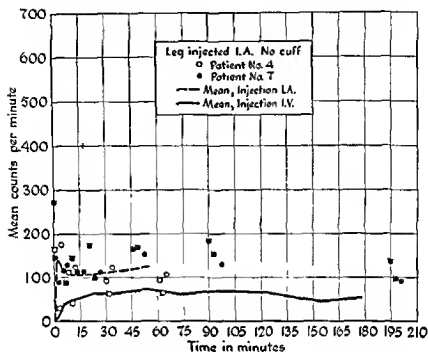


Fig 4—Radioactive phosphorus present in legs injected intra-arterially with no blood pressure cuff

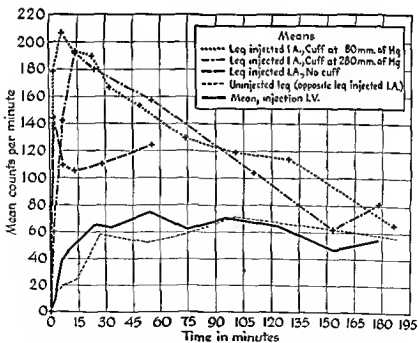


Fig 5—Mean curves of radioactive phosphorus present in injected legs using intravenous injection and the three different intra-arterial methods of injection

TABLE II. MEAN VALUES OF GEIGER COUNTER DETERMINATIONS OF RADIOACTIVE PHOSPHORUS IN THE TOP, DORSUM, AND MIDDLE OF THE LEGS AFTER INTRAVENOUS INJECTION INTO THE LEFT ANTERIOR VAIN OF TWO NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	12	0	0
5 to 3	10	2	10
4 to 7.5	9	6	38
8 to 12	9	10	46
14 to 28	10	21	65
31 to 36	10	33	62
51 to 56	4	51	74
71 to 80	11	75	62
90 to 100	12	91	70
120 to 127	12	123	64
150 to 157	6	154	46
170 to 187	10	179	54

TABLE III. MEAN VALUES OF GEIGER COUNTER DETERMINATIONS OF RADIOACTIVE PHOSPHORUS IN THE TOP, DORSUM, AND MIDDLE OF THE INJECTED LEG USING THE INTRA-ARTERIAL METHOD WITH THE CUFF AT 60 MM. Hg. IN THREE NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	9	0	0
5 to 4	9	2	174
6 to 10	9	7	208
11 to 17	10	14	193
19 to 27	7	23	190
29 to 36	6	32	167
46 to 52	6	49	137
69 to 80	6	74	129
90 to 108	6	100	119
120 to 139	6	129	111
182 to 190	6	186	65

TABLE IV. MEAN VALUES IN THE TOP, DORSUM, AND MIDDLE OF THE INJECTED LEG USING THE INTRA-ARTERIAL METHOD WITH THE CUFF AT 280 MM. Hg. IN THREE NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	9	0	0
1 to 4	9	2	60
5 to 9	10	7	142
11 to 19	9	11	192
20 to 29	9	24	180
40.5 to 71	9	55	157
91 to 126	6	110	104
150 to 156	3	153	62
175 to 181	3	178	81

TABLE V. MEAN VALUES IN THE TOP, DORSUM, AND MIDDLE OF THE INJECTED LEG USING THE INTRA-ARTERIAL METHOD WITH NO CUFF IN TWO NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	6	0	0
5 to 5	6	2	144
6 to 8	7	7	109
9 to 17	6	13	105
21 to 34	6	28	110
46 to 63	6	53	124

TABLE VI. MEAN VALUES OF GEIGER COUNTER DETERMINATIONS OF RADIOACTIVE PHOSPHORUS IN THE TOE, DORSUM, AND MIDCALF OF THE UNINJECTED LEG (OPPOSITE LEG INJECTED INTRA-ARTERIAL) WITH THE CUFF AT 80 MM Hg IN THREE NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	9	0	0
1 to 5	9	3	15
6 to 15	3	7	20
9 to 18	11	13	23
20 to 37	12	28	49
47 to 53	6	50	43
70 to 81	6	75	54
91 to 109	6	100	67
121 to 190	6	130	55
183 to 191	6	187	51

TABLE VII. MEAN VALUES IN THE TOE, DORSUM, AND MIDCALF OF THE UNINJECTED LEG WITH THE CUFF AT 280 MM Hg IN THREE NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	9	0	0
1 to 4	7	2	5
5 to 9	6	7	20
12 to 18	8	14	27
20 to 30	9	25	56
48 to 54	6	51	63
65 to 73	3	69	65
96 to 102	3	99	63
121 to 127	3	124	41
151 to 157	3	154	38
176 to 182	3	179	40

TABLE VIII. MEAN VALUES IN THE TOE, DORSUM AND MIDCALF OF THE UNINJECTED LEG WITH NO CUFF IN TWO NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	6	0	0
1 to 6	6	3	12
10 to 18	6	14	22
22 to 35	6	29	50
47 to 66	6	57	52
91 to 100	3	95	89
106 to 202	3	199	80

TABLE IX. MEAN VALUES OF THE UNINJECTED SIDE OF ALL VALUES OF THE TOE, DORSUM, AND MIDCALF IN TABLES VI, VII, AND VIII

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	24	0	0
2 to 3	21	3	15
6 to 9	9	7	20
13 to 14	25	14	24
25 to 29	27	27	58
50 to 57	18	53	52
69 to 75	9	73	58
93 to 100	12	99	71
179 to 199	12	188	55

twice the maximum values obtained by injection without a cuff for a period of thirty minutes. The maximum values with a cuff fell to maximum values without a cuff at one and one-half hours, indicating that the stasis by the cuff gives a higher concentration locally for one and one-half hours. With the cuff at 2-0 mm. of mercury the minimum values remained below the mean for the intravenous method for thirty minutes, indicating that the phosphorus may be withheld from the leg in certain cases during this time. This suggests that the cuff at 80 mm. of mercury will give more consistent results.

*Penicillin Dosage*—Fortunately, in infections of the extremities, the bacterial flora is usually sensitive to penicillin, and with a local infection of a portion of the body such as an extremity, the permeability of the local area is the determining factor. Therefore, the method of administration of the penicillin is the important variable rather than the dosage. On this basis an empirical dosage of 50,000 Oxford units of penicillin dissolved in 10 c.c. of saline solution has been used as suggested by Glasser and associates.<sup>14</sup> In several of the series, this dosage was given in 5 c.c. of saline solution, but since the dilution to 10 c.c. gives a solution with a pH equal to that of blood (7.4), the latter has been used recently, although no difference was noted clinically in the effects. The injections have been given once or twice daily. No improvement in the results was noted in cases in which intramuscular penicillin was given concomitantly.

*Technique*—In most cases, particularly in those involving the feet and lower portion of the legs, a constant regimen is used. The patient is given 1 gr. papaverine hydrochloride hypodermically twenty minutes prior to the intra-arterial injection to aid in the vasodilation of the extremity since circulatory impairment is frequent in these cases. A second adjunct consists of soaking the foot (and leg) in a warm 1:9000 potassium permanganate solution for twenty minutes prior to the injection. This has the fourfold effect of aiding the cleansing and effecting better drainage in necrotic stumps, toughening the adjacent normal skin, and preventing ulceration; second, it is one of the best fungicidal agents known and effectively controls the epidermophytosis, which frequently accompanies or in many cases actually causes the onset of the foot infection<sup>15</sup>; third, potassium permanganate acts as an excellent deodorant in gangrenous extremities<sup>16</sup>; and last, the warmth of the solution also aids as a temporary vasodilator immediately prior to the intra-arterial injection. For the injection, a 20 c.c. syringe with an attached 20 gauge needle 2½ inches long is used. A blood pressure cuff is placed just above the knee with the center of the cuff over the medial aspect of the thigh. The cuff is inflated to a subdiastolic blood pressure (60 to 80 mm. of mercury). With the surgeon standing on the right side of the patient the point of maximum pulsation of the femoral artery on the involved side below the inguinal ligament is palpated with the left hand, and the artery stabilized with the index and middle fingers (Fig. 6). The injection is done most easily in a plane perpendicular to the leg rather than at an acute angle. Proximity to the artery is noted by arterial pulsation transmitted to the syringe. A bright red stream pulsating into the syringe denotes that the needle is within the lumen of the artery. The color of the blood may vary in

different individuals but a good intermittent pulsation is taken as positive evidence of arterial blood. Care taken not to introduce the needle to too great a depth after getting within the lumen will obviate a transfixion of the artery and is easier than introducing the needle at an angle. Injections are done at a rate of 1 c.c. per second, and, immediately after withdrawal of the needle, digital pressure is applied over the site for a few seconds to obviate hematoma formation. In the case of the upper extremity, the blood pressure cuff is applied proximal to the infection (usually at some site above the elbow) and inflated to 80 mm. of mercury. Then the injection is made either at the brachial artery of the elbow or at the distal portion of the axillary artery. The blood pressure cuff is maintained at 80 mm. of mercury for ten minutes.

Although several of the patients have responded well to a total of only one or two injections, one or two doses daily are usually continued until optimal results are achieved.



Fig. 6—Technique of intra-arterial injection. Note pulsation of arterial blood into the syringe.

*Therapeutic Application of Proposed Intra-arterial Regimen.*—Intra-arterial penicillin and the proposed regimen have been used in forty cases of multiple types of infections of the extremities with excellent beneficial results. Diabetic gangrene and gangrene due to arteriosclerosis and frostbite with associated infection, osteomyelitis, suppurative joints, infected ulcerations of the legs and feet, and infected operative incisions have all responded well to this mode of therapy. Diabetic gangrene presents a problem in which the triad of diabetes, infection, and vascular impairment is met. Intra-arterial penicillin is presented as the most effective means of controlling the element of infection and will, of course, do the most for the patients with a severe infection who have an adequate circulation. After the infection has been controlled, several days may be devoted to improving the patient's general status by blood or plasma transfusions and a high protein regimen such as the Vereo diet.<sup>24</sup> Amputation is considered



eradication of a recurrent cellulitis which had progressed over a three-week period while the patient was given well over 2 million units of intramuscular penicillin.

**CASE 2**—H. R., a 65 year old woman, had diabetic arteriosclerotic gangrene of the right third toe, cellulitis and edema of the entire right foot, a destructive osteomyelitis of all the phalangeal bones of the third toe and second and third metatarsals, and a temperature of 100.4° F. Routine intra arterial penicillin therapy was given twice daily for four days at which time the edema and cellulitis had disappeared from the foot. A local amputation of the third toe was done and an adjacent sinus tract and abscess were opened. The cartilage on the articular surface of the third metatarsal was excised but the metatarsals involved by osteomyelitis were not otherwise disturbed. Five intra arterial injections of penicillin were given during the first four postoperative days, and the wound was very clean at that time. The only further therapy was the application of sterile dressings. The end of the foot was completely healed three weeks postoperatively, and the patient has been ambulatory during the four months since that time.

*Comment*—Control of soft tissue infection and osteomyelitis made possible a successful local amputation in this case.

**CASE 3**—G. Y., a 66 year old woman had diabetic arteriosclerotic gangrene with vesiculation and necrotic ulcerations of the foot and lower right leg, and edema, increased heat, mottling, and palpable venous thromboses extending to the upper third of the right leg. The temperature was 101° F and the pulse was 120 per minute. An abscess on the lateral side of the foot was opened and the patient given intra arterial penicillin twice daily, the temperature stayed below 99.6° F after forty eight hours of therapy. A local amputation on the foot was done on the fourth day but an ischemic necrosis continued in progress although no infection was present. A supracalcaneal amputation was then done with primary closure of the wound after an intra arterial penicillin injection had been given immediately preoperatively. Adequate preoperative preparation of the patient made possible a smooth operative course with little change in the pulse or blood pressure in spite of the fact that no blood or plasma was used during the procedure or postoperatively. The stump healed by primary intention in ten days.

*Comment*—Preoperative control of infection in this toxic case of diabetic gangrene by intra-arterial penicillin facilitated surgery and permitted primary healing of the closed amputation.

**CASE 4**—H. B., a 63 year old man, had diabetic gangrene with pitting edema and erythema of the entire left foot, a deeply penetrating necrotic ulcer at the base of the left fifth metatarsal, and a gangrenous ulceration 4 by 4 by 5 cm in size on the lateral dorsal portion of the foot. Culture of the purulent exudate revealed hemolytic streptococci and coagulase negative staphylococci. Conservative soft tissue debridement of the connecting dorsal and plantar areas was done, and the patient was given twenty injections of intra-arterial penicillin over thirteen days. The wound was clean and granulating at this time and one week later the plantar area was healed. The dorsal area of defect was then punch grafted and nine tenths of the punch grafts took. The foot was well healed eleven days after the grafting and the patient has been ambulatory and had no further difficulty during the four months since that time.

*Comment*.—Control of infection in this case of diabetic gangrene made it possible to save the foot and successfully skin graft an area which had previously been gangrenous.

**CASE 5**—L. M., a 66 year-old woman, was admitted with generalized arteriosclerosis, terminal renal arteriosclerosis, and wet gangrene of the entire right hallux and two inches of







Fig 7

Fig 8

Fig 7 (Case 7)—Marked cellulitis and edema of left foot prior to therapy (note pitting edema of dorsum of foot).

Fig 8 (Case 7)—Left foot after forty-eight hours of therapy, revealing disappearance of cellulitis and edema.



Fig 9 (Case 7)—Stump of left hallux healed by primary intention of twelfth postoperative day.

intra arterial injections were given during the following week and portions of necrotic tendons sloughed spontaneously. The toe was then amputated through the proximal phalanx under intra arterial procaine anesthesia using 25 cc. of 2 per cent procaine with 50,000 units of penicillin added. After this injection the *Das Santo* stress technique was used in which the cuff was inflated to 280 mm. of mercury and hemostasis was accomplished during the procedure. A primary closure of the amputation stump was done. No pain or discomfort was experienced by the patient during the procedure. Post-operatively the patient was given six routine intra arterial penicillin injections and the stump healed by primary intention (Fig 9). Subsequent roentgenograms of the left foot revealed no residual osteomyelitis in the stump of the phalangeal bone of the hallux.

*Comment.*—The subsidence within twenty-four hours of a severe cellulitis of the leg which extended up to the knee and the subsequent primary healing of an amputation done through an area of osteomyelitis in the toe demonstrates the rapidity and efficacy of intra-arterial penicillin therapy.

*CASE 8*—J. P., a 62 year old non-haemic woman, had cardiac failure and arteriosclerotic gangrene of both feet. A massive gangrene of the right foot and lower third of the leg was present with cellulitis and edema extending up to the knee. Dry gangrenous areas with surrounding cellulitis were present on the left second and third toes, medial malleolus, and heel. Cultures revealed hemolytic streptococci, coagulase-negative staphylococci, and aerobacter. Six intra arterial penicillin injections of 50,000 units each were given bilaterally over five days. The cellulitis regressed to a point two-thirds up the right leg after twenty four hours and no cellulitis was evident on either leg after forty-eight hours. A steady fall in the leucocyte count occurred, from 21,000 to 9,000, over six days of therapy. The gangrenous portions of the toes on the left foot sloughed spontaneously and all infection cleared. A definitive closed right supracondylar amputation was done and the stump healed by primary intention. Pathologic examination of the specimen revealed organized thrombi in all three major arteries of the lower right leg and 90 per cent occlusions of the popliteal artery.

*Comment*—Infection in a massive arteriosclerotic gangrene was controlled in spite of the occlusion of all three main arteries of the lower leg and a definitive supracondylar amputation healed by primary intention.

*CASE 9*—A. H., a 40 year old woman, had gangrenous areas due to frostbite on the medial three toes of each foot and both heels, a severe cellulitis of the feet, and systemic toxicity with the temperature elevated to 103.6° F. She was given nine intra arterial penicillin injections over a period of six days, at which time she was afebrile, the cellulitis had disappeared, and the dry gangrenous areas were demarcating well. A considerable portion of the dry gangrenous areas sloughed spontaneously during the next six days, at the end of which time the patient was given 50,000 units of penicillin in 50 cc. of 1 per cent procaine into the femoral artery with the blood pressure cuff, which subsequently pumped 280 mm. of mercury. Then a removal of the remaining eschar and an amputation of the distal half of the distal phalanx of the second left toe were done painlessly without additional anesthetic agents. Both feet had healed completely one month later.

*Comment*—The infectious element was effectively controlled in this case of gangrene due to frostbite and a demarcation of a smaller area of dry gangrene permitted so that only a small local amputation was necessary.

*CASE 10*—M. S., a 79 year old woman, was admitted with diabetic arterio-sclerotic gangrene of both feet. There was a wet gangrene of the right second toe and 2 cm. of the adjacent foot, and a dry gangrene of the distal one-fourth of the left second toe. A culture of the right foot revealed gram positive cocci, *Esch. coli*, *Proteus*, and *Aerobacter*. Roentgenograms revealed calcification of the arteries of the foot, osteomyelitis of the right second middle

and proximal phalanges, and left second proximal phalanx. A routine regimen of intra-arterial penicillin (50,000 Oxford units), papaverine, and potassium permanganate foot soaks (1:9000 concentration) was given bilaterally twice daily for a total of fourteen injections. The area of wet gangrene on the foot regressed, and an amputation of the second right toe was then done through the area of osteomyelitis in the proximal phalanx. This site was chosen to determine whether or not the penicillin had eradicated the bone infection. The wound was closed secondarily twelve days later since this was an early case, and the full benefits of the therapy were not yet appreciated. Healing was slow but complete in less than two weeks. The gangrenous portion on the second left toe sloughed spontaneously, and the toe healed completely with a small scar prior to discharge. A recheck x-ray examination of the right foot, two months later, revealed no evidence of osteomyelitis in the amputated stump of the proximal phalanx. During the more than one-half year since hospital discharge, the patient has been ambulatory and has had no further difficulty.

**Comment.**—Complete arrest of infection by intra-arterial penicillin has permitted the site of a right second toe amputation for gangrene to remain healed for over one-half year although the amputation was done through an area of osteomyelitis, the foot had been involved by wet gangrene, and the interdigital arteries of the foot were revealed by roentgenogram to be calcified.

**CASE 11.**—R. A., a 19-year-old man, developed a postoperative infection of the left knee joint following the operative removal of a torn anterior cruciate ligament and medial meniscus. The septic course followed subsequently is shown in Fig. 10. Cultures of the purulent exudate revealed coagulase-positive staphylococci to be present. Multiple therapeutic measures including three courses of high dosages of intramuscular penicillin, and one course of oral sulfadiazine, gave no beneficial results over a period of seven weeks. However, sensitivity tests on the strain of staphylococcus present in the pus at this time revealed the organism to be inhibited by a penicillin concentration (Pfizer 125) of 8 units per cubic centimeter. Intra-arterial penicillin was started at this time and twelve injections were given over nine days. The severe suppurative arthritis healed completely in eighteen days. Physiotherapy started two weeks after this time resulted in no flare-up of the infection and the patient was able to flex the knee 20 degrees prior to hospital discharge.

**Comment.**—The failure of high dosages of intramuscular penicillin is attributed to the tissue barriers of the knee which excluded local permeation of the drug and prevented success although the *Staph. aureus* present was susceptible to penicillin as shown in sensitivity tests. Intra-arterial administration of penicillin overcame this tissue barrier and made control of the infection possible.

**CASE 12.**—A. E., a 63-year-old diabetic man, had moderate arteriosclerotic cellulitis of the dorsum of the foot and a painful perforating infected ulcer on the sole of the left foot of three months' duration. Culture of the purulent exudate revealed coagulase-positive staphylococci and aerobacter. An area of callus surrounding this ulcer was excised and potassium permanganate foot soaks, papaverine, and intra-arterial penicillin were given twice daily for five days. The cellulitis on the dorsum of the foot disappeared in two days, and the ulcer healed in one week, but the patient was not allowed to bear weight on the foot for two weeks. In the four months since that time the patient has been able to walk on the foot without pain or recurrent ulceration.

**Comment.**—Diabetic perforating ulcer of the sole of the foot usually resistant to therapy healed rapidly on intra-arterial penicillin therapy.

**CASE 13.**—I. S., a 32-year-old woman, had an enlargement of the entire left leg secondary to an old thrombophlebitis, large superficial varices, and a chronic deep ulceration

over the left medial malleolus with hemolytic streptococci present. A venogram revealed a thrombosis of the saphenous vein in the lower leg adjacent to the ulceration, but a patent deep circulation. Three intra-arterial injections of 50,000 units each were given during the forty eight hours prior to surgery and then 200,000 units of penicillin injected down the saphenous vein, a high saphenous ligation and an excision of the ulcer were done under spinal anesthesia. A split thickness skin graft placed over the ulcer on the sixth day had a 95 per cent take.

*Comment*—Successful skin grafting of a chronic thrombophlebitic ulcer with hemolytic streptococcal infection was facilitated by proper penicillin therapy.

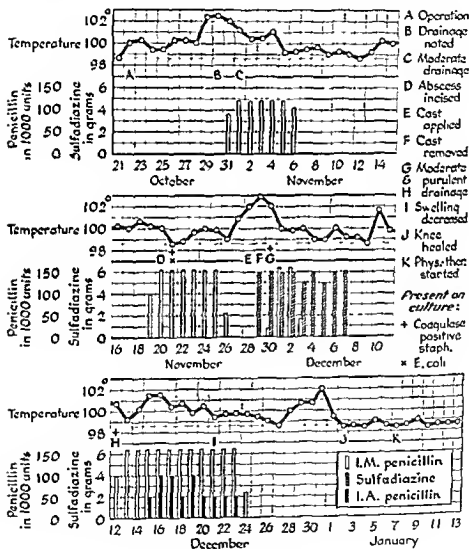


Fig 10 (Case 11).—Course during hospitalization.

**CASE 14**—J. D., an 18 year old girl, with a proved diagnosis of acrocyanosis had previously had sympathectomies on all four extremities. In spite of this a necrotic ulceration had developed on the first and second left toes at a site of infection and had been unresponsive to various local medicaments tried over a two week period. Neither the dorsalis pedis nor the posterior tibial artery of the foot was palpable. Culture of the pus revealed hemolytic streptococci and coagulase negative staphylococci to be present. The ulcer was debrided and two intra arterial injections of penicillin were given, resulting in a disappearance of the infection within three days.

*Comment.*—Intra-arterial penicillin effectively cleared the infection in a foot ulcer in a patient with acrocyanosis in spite of the impaired blood supply to the area.

**CASE 15**—F. H., a 45 year old man, had a cellulitis, paronychia, and subungual abscess of the right thumb. Temperature was 100.8° F and the pulse 110. The leucocyte count was elevated to 14,500. He was started on full therapeutic doses of sulfadiazine (1 gm every four hours) and drainage of the abscess was effected by incision and removal of the radial third of the thumbnail. Temperature returned to normal within twenty four hours but three days later an erythema of the distal two thirds of the distal phalanx with marked tenderness of the center of the palmar aspect indicative of an infection of the distal closed space of the thumb (felon) developed. Sulfadiazine was stopped and the patient was given one injection of 50,000 units of penicillin into the right brachial artery. Within forty eight hours all inflammation and tenderness were controlled without incision of the felon. The patient had no further difficulty with the thumb.

*Comment.*—A felon which developed while the patient was on sulfadiazine therapy cleared completely in forty-eight hours without incision after one intra-arterial injection of penicillin (50,000 units).

**CASE 16**—A. K., a 32 year old physician, developed an infection of the left index finger and a tubular lymphangitis of the arm a few hours after he had accidentally pricked himself while operating on a patient with gas gangrene and hemolytic streptococcus cellulitis of the abdominal wall. Within twelve hours the temperature was elevated to 103° F and the condition was toxic. He was then given 50,000 units of penicillin intra arterially into the left axillary artery. Twelve hours later the cellulitis was receding, but intramuscular penicillin was started (20,000 units every three hours) as an additional precautionary measure. Local inflammation had disappeared by thirty six hours and he was afebrile by forty eight hours. However, the patient from whom he had contracted the infection died of a fulminating gas gangrene of the abdominal wall in spite of intramuscular penicillin therapy and additional measures. The physician left the hospital in four days with no residuals.

*Comment.*—Rapid control of an acute fulminating infection of an arm was possible by intra-arterial and intramuscular penicillin in this case.

**CASE 17**—A. G., a 70 year old diabetic woman, had developed a severe postoperative infection following a bunion operation done elsewhere. A severe osteomyelitis and cellulitis progressed in spite of therapy and the patient was referred for amputation two months later. Physical examination at this time revealed a purulent draining operative incision with surrounding ulceration of the skin of the medial side of the foot and a cellulitis of the dorsum of the foot. Roentgenogram of the foot revealed a severe osteomyelitis at the operative site (Fig 11). Intra arterial penicillin, papaverine, and potassium permanganate foot soaks were given twice daily and all cellulitis disappeared in forty eight hours. All drainage ceased by the sixth day. Intra arterial penicillin was continued, however, until thirty injections had been given. The epithelium grew in well, and six weeks after the start of the therapy the skin had epithelized over the area. The patient has walked on the foot for five months.

since then with no pain or signs of recurrent infection. Roentgenogram of the foot at this time revealed a good bony union at the operative site with no evidence of osteomyelitis (Fig 12).

**Comment**—A severe wound infection, cellulitis, and osteomyelitis following a bunion operation responded well to intra-arterial penicillin.

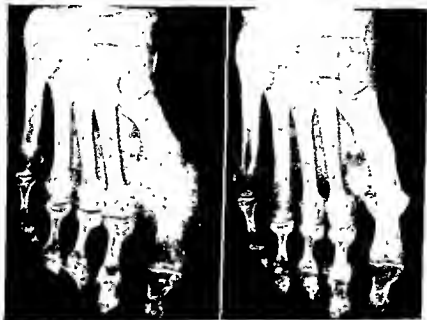


Fig 11

Fig 12

Fig 11 (Case 17)—X-ray of right foot revealing marked osteomyelitis present at first metatarsophalangeal junction with soft tissue swelling of foot.

Fig 12 (Case 17)—X ray revealing good bony union with no evidence of osteomyelitis five months after hospital discharge.

#### *Discussion of Possible Objections and Contraindications to the Technique*

Because of the frequency with which veins are used for infusions rather than arteries, there may be a natural antipathy on the part of the clinician toward arterial puncture. This misconception has no basis in fact, since the distributing arteries are usually much more suitable anatomically than their concomitant veins for repeated puncture. Thus, in the histology by Maxamov and Bloom,<sup>21</sup> we note that, "The wall of the veins is always thinner, softer, and less elastic than that of the arteries." The better development of muscular and elastic tissue in arteries as opposed to the greater prominence of connective tissue in the veins is also mentioned. In the arteries, the internal elastic membrane adjacent to the tunica intima is very well developed and acts as an efficient self-sealing mechanism. Evidence of this efficiency can be deduced from Case 17 in which a 70 year-old woman received a total of thirty intra-arterial injections at approximately the same site in the common femoral artery over a period of sixteen days without hematoma formation or any other difficulty. Similarly, there has been no incidence of hematoma formation in any of the other patients treated.





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## THE IMPORTANCE OF PRECISE BACTERIOLOGIC DATA IN THE TREATMENT OF INFECTIONS OF THE UROGENITAL TRACT

JOSEPH A. LAZARUS, M D, AND LEWIS H. SCHWARZ, B S, NEW YORK, N. Y.

GREAT strides have been made in the diagnosis and treatment of diseases of the urogenital tract within the past ten years. It seems to us, however, that we are now entering an era when even greater advances will be made in treating urinary tract infections, because of phenomenal discoveries in the fields of antibiotics and chemotherapy.

Until recently the treatment of urinary tract infections has been more or less haphazard and empirical, primarily because of (1) failure to identify causative organisms of infections, (2) nonavailability of, or failure to use, drugs capable of destroying offending organisms, and, finally, (3) failure to relieve concomitant obstructions impairing free urinary drainage.

A fully equipped bacteriologic laboratory staffed by a competent bacteriologist, especially as it pertains to the treatment of infectious uropathies, has become an indispensable accessory in the practice of modern urology. The time has passed when urologists were willing to accept reports from laboratories giving group designations of organisms instead of specific identifications. To state, for example, that a sterilely obtained specimen of urine shows a growth of *Bacillus pyocyaneus*, without testing its behavior in vitro, can result in a false conception regarding pathogenicity and, at times, lead to dire results because of inadequate treatment.

A patient (Mr. J. P.) was operated upon by the senior author (March, 1940). A right nephrectomy and subtotal ureterectomy were performed for suppurative pyelonephritis, ureteritis, and multiple renal calculi. During the course of a routine follow-up urologic examination (April 9, 1946), a gram-negative encapsulated rod was discovered on culture in the bladder urine specimen. Urine from the left kidney was negative on smear and sterile on culture. The colony appeared mucoid, was distinctive because of its heaped-up character, and was distinctly hemolytic. Although the organism presented close similarity to the Friedlander bacillus, we deemed it advisable to carry out further studies. When inoculated into Kligler's iron agar, it became immediately evident that we were not dealing with a Friedlander bacillus because of the negative butt and slant, indicating lack of acid and gas formation. Following inoculation of routine differential media the organism was ascertained to be a mucoid variant of *Pseudomonas aeruginosa* (*B. pyocyaneus*). Due to the similarity of this organism to *Pseudomonas fluorescens*, differentiation could be made only by establishing the pathogenicity through animal inoculations. In vivo studies readily disclosed that we were dealing with a virulent organism of great toxicity which promptly killed all animals used in the examination. A careful assay was then carried out which disclosed that the growth of this or-

ganism was inhibited by streptomycin, but was in no way influenced by penicillin or the sulfonamides.

For several years reports have been received, in which the causal organism was called *Staphylococcus albus* until one of us (L. H. S.) began the routine use of differential media as a means of specific identification of bacteria. We were surprised to find that what on casual inspection appeared to be a *Staph. albus* was actually a *Staph. aureus*. The reason for this error was that colonies of *Staph. aureus* grown on agar plates frequently appear white on mere inspection. Careful scrutiny of these colonies, however, usually discloses a faint yellowish tint. The exact nature of the bacterium is readily ascertained from its behavior on differential media.

One of the most common organisms apparently isolated in the urine is the *Bacillus coli*, with no further descriptive elaboration from the bacteriologist. Yet, the designation *B. coli* is indefinite because of the multiplicity of organisms constituting this group. Most bacteriologists plate specimens on eosin-methylene blue, agar, with the result that any colony which presents a metallic sheen is classified in the group of *B. coli*. It should be recalled, however, that any organism which ferments lactose will form this variety of colony when grown on this agar. The two groups of organisms falling within this category are aerobacter and escherichia. The former, which comprises such organisms as (1) *Aerobacter aerogenes*, (2) *Aerobacter cloacae*; and (3) *Aerobacter sp.* (an heterogeneous group), should not be classified as *B. coli* because the latter group, which consists of *Escherichia coli* (communis and communior) and *Escherichia freundii*, constitute the true members of the *B. coli* category. Although members of both categories may invade the urogenital tract and cause great pathologic changes, the first is usually associated with the gastrointestinal tract, while the second is a common cause in infections of the urinary tract. As a rule both groups are readily destroyed by the sulfonamides and by streptomycin, but are unaffected by penicillin.

For several years the subject of amicrobial pyuria has been discussed in medical literature. We are all undoubtedly aware that a sterily obtained specimen of urine containing leucocytes, which fails to show organisms on smears, must be carefully examined for the mycobacterium of tuberculosis, especially in acid urines. The absence of this organism and failure to obtain a growth on the commonly employed aerobic culture media has led observers to group such examples in this category. It seems to us, however, that before doing this, specimens should be cultured on carefully selected anaerobic media. There are approximately twelve anaerobic organisms, ranging from micrococci to the gram-negative nonspore-forming rods, and including one member of the Neisserian group, which are obligate anaerobes showing pathogenic features when invading the genitourinary tract. It is our routine to use anaerobic media whenever urines fail to show organisms upon routine aerobic media, and upon all urines obtained from patients who present symptoms suggestive of urinary tract infection regardless of the presence of cellular elements in the urine. We have in mind supplementary reports regarding this subject to be published in the near future.



**Laboratory Procedures.**—Upon examination of specimens, urine specimens, preferably freshly procured, should be collected into two tubes, one for smears and the other for culture. Negative smears of a thoroughly centrifuged urine specimen do not necessarily, as aforesaid, indicate absence of bacteria. We have repeatedly found this to be the case, and *contrary to what has frequently been advocated*, we routinely culture all urines, regardless of the results of the smears. Failure to follow this procedure and to rely upon smear diagnoses, that is, making gram stains of smears taken from growths on culture media, often leads to errors in diagnosis. For example, an orange yellow colony is frequently seen on plates, which upon the stained smear discloses cocci in small clumps. Failure to employ differential media may lead to calling this *Staph aureus*, whereas if it were run through the media it would be found to be *Micrococcus aurantiacus*. In the same manner, *Micrococcus cereus* may be mistaken for *Staph albus*, except that the former does not liquefy gelatin. All of these organisms are pathogens and have been isolated from foci of infections, yet not all of them respond similarly to chemotherapy. It is, therefore, important that differential media be used, as well as that chemotherapeutic assays be run in order to ascertain the sensibility of bacteria to drugs.

When urines are inoculated into broth media, it is frequently found that in the presence of a multiplicity of organisms the bacteria showing the most luxuriant growth propensity completely overgrow all others, making it impossible on the subsequently transplanted agar plates to isolate and thereby identify the various bacterial colonies present. For this reason we have found it advantageous immediately to streak blood agar plates at the same time that the broth media are inoculated. Differential media and in vitro examinations are made routinely.

Whenever an organism is isolated which fails to conform to the usual standards, animals are inoculated and further examinations made. Only in this way can the bacteriologist determine the behavior and pathogenicity of the unusual causal organism. Careful assays must be made occasionally in order to ascertain the toxicity of bacteria, as well as the effect that specific therapy may exert upon them. A common method used by laboratories in order to ascertain pathogenic tendencies of bacteria is to determine the capacity of the organism to hemolyze blood agar. Yet, it is common knowledge that many saprophytes also show this tendency by virtue of their ability to hemolyze blood through metabolic processes. On the other hand, it is also known that many pathogens fail to show this tendency. Animal inoculation is the only certain method of determining the degree of pathogenicity of bacteria.

**Adaptation of Drug to Organism.**—With specific therapeutic agents becoming available in ever-increasing numbers, it becomes necessary for the urologist to ascertain, whenever treating infections of the urogenital tract, not only the adaptability of antibiotics to the nature of offending organisms, but also the correct dosages required to achieve adequate results. The tendency to rely on instructions furnished by drug manufacturers in the use of chemotherapeutic agents or on the opinions of writers in their various publications is not desir-



or penicillin by their physicians long before they have been subjected to urologic examinations and before any attempt was made to identify the causal organism of infection. We have received innumerable requests from patients as well as physicians for information regarding the use of drugs which would cure urinary infections. They are frequently surprised when asked whether the urine has been cultured, stating that they believed this to be an unnecessary procedure in view of the availability of such "wonder drugs" as sulfonamides, penicillin, and especially the "mysterious superdrug" streptomycin, glowing accounts of which they read in newspapers or medical periodicals. It makes little difference to the average physician, when using penicillin, whether the organism is a member of the *B. coli* group or a virulent strain of *pyocyaneus* or *Bacillus proteus*, little realizing that these organisms are not affected by this drug. But the outstanding risk of the indiscriminate use of chemotherapeutic drugs is not so much the deleterious effects which they may have on the patient, but rather the dangerous effects of the drugs in provoking a state of resistance by the patient to the particular drug, so that should subsequent circumstances make it exigent to use drugs against an organism known to be susceptible to them, their potency will be greatly nullified by the induced resistance of the patient.

Likewise, if correctly selected drugs within this category are used in insufficient dosages, organisms may readily develop an immunity to them, so that within a short time they are no longer inhibited. In other words, a good rule to follow when using antibiotics is to select a drug that is known to be specific for causal bacteria and to use it in sufficient dosage to destroy them promptly and permanently.

#### SUMMARY AND CONCLUSIONS

With the advent of chemotherapy, the treatment of urogenital infections has become completely dependent on the bacteriologic laboratory. We can no longer remain indifferent to the causative organism when treating infections. Urologists must insist upon precise identification of bacteria rather than upon group designations, because members of the same species of bacteria may show decided variations in pathogenicity and reactivity to drugs generally considered specific for the species. This requires constant access to a well-equipped laboratory and the work of a competent bacteriologist who is capable of carrying out *in vitro* and *in vivo* studies of bacteria, as well as accurate assays on the toxicity of organisms, their reaction to drugs, and the most effective dosages required to exterminate them.

To avoid contaminating urine specimens, careful attention must be paid to maintaining asepsis in obtaining specimens from the bladder and kidneys. The use of strong antiseptics capable of sterilizing urines at the source and during transport must be circumspectly avoided.

We have attempted to outline the routine used in our laboratory of obtaining and examining urine specimens, with the view of showing the need of bacteriologic laboratory facilities as essential features in the office armamentarium of the urologist. The prompt and frequent culture examinations of freshly procured urine specimens, without subjecting patients to financial





## THE POSTGASTRECTOMY SYNDROME

DAVID ADLERSBERG, M.D., AND ERNST HAMMERSCHLAG, M.D., NEW YORK, N. Y.  
(From the Nutrition Clinic and the Medical Services of The Mount Sinai Hospital)

**S**UBTOTAL gastrectomy is considered to be the method of choice for surgical treatment of peptic ulcer. Jejunal ulcer is an occasional postoperative complication of this operation, whereas it is exceedingly common after gastroenterostomy. A group of patients, however, present a variety of complaints and symptoms after gastric resection even though they do not have peptic jejunal ulcers. This clinical observation is confirmed by comprehensive follow-up studies. In a group of ninety-four partially gastrectomized patients, studied by Sarah Jordan,<sup>1</sup> twenty-seven (29 per cent) had difficulties in maintaining normal weight and presented a definite nutritional problem. Mateer<sup>2</sup> estimated that approximately 14 per cent of his patients showed postprandial symptoms. Miller<sup>3</sup> found in 17 of 240 cases symptoms of weakness, pallor, and loss of weight. Custer, Butt, and Waugh<sup>4</sup> encountered in 26 of 200 cases postprandial symptoms; in twelve cases these symptoms were mild, in ten they were severe and interfered with the daily work of the patients, and the six remaining patients were classified as "gastric cripples" because of their complete inability to work. Berkman and Heck<sup>5</sup> studied extensively the postprandial distress after gastric resection, the so-called dumping syndrome. The distress was more severe in the first two months after the operation than at a later period. In some instances aversion to food developed, the eating habits deteriorated, and this resulted in the consumption of only minimal amounts of food. Sandweiss and associates<sup>6</sup> agreed with Crohn<sup>7</sup> and others, that gastric resection is at present the operation of choice for peptic ulcer but emphasized the importance of postoperative gastrointestinal symptoms without marginal ulcer. In their opinion some of the patients are more incapacitated than those who have recurrent ulcers. Although the number of these patients is fortunately comparatively small, a careful study of their symptoms and signs would appear to be well justified.

During the past three years a group of fourteen patients who underwent subtotal gastric resection was studied at the Nutrition Clinic of Mount Sinai Hospital. All fourteen patients were markedly underweight and were referred to the clinic as nutritional problems. After a thorough clinical examination including x-ray studies and laboratory analyses, various types of high caloric, high protein, high vitamin diets were given, as well as vitamin concentrates and liver extract. The therapeutic results, however, remained, as a rule, unsatisfactory. During the course of the observations a study of the underlying causes of the postgastrectomy syndrome was carried out in each case.

### GENERAL CHARACTERISTICS

The group includes thirteen patients with subtotal gastrectomy for peptic ulcer and one case of total gastrectomy for gastric syphilis. Of the thirteen ulcer cases, ten patients had had preoperatively duodenal ulcer and only three a gastric ulcer. Patients who had had resections for carcinoma of the stomach



TABLE II. OCCURRENCE OF SYMPTOMS

NO.	NAME	WEAKNESS FATIGUE	POST PRANDIAL FULNESS AND OR NAUSEA	ERUCTA TION AND BELCHING	DIZZI NESS	CONSTIPA TION	DEAR RHEA	VITAMIN DE FICIENCY
1	C. M.	+	+	+	+	+	-	-
2	G. H.	+	+	+	+	+	-	-
3	L. Z.	+	+	+	+	+	-	-
4	J. K.	+	+	+	+	+	-	-
5	M. I.	+	+	+	+	-	-	+
6	S. B.	+	+	+	+	-	-	-
7	S. Z.	+	+	+	+	-	-	-
8	B. I.	+	+	+	+	+	-	-
9	B. H.	+	+	+	+	+	-	-
10	I. H.	+	+	+	+	+	+	-
11	F. M.	+	-	+	+	-	-	-
12	B. H.	+	-	-	-	-	+	+
13	A. F.	+	+	+	+	+	-	+
14	G. S.	+	+	+	+	+	+	-

teen patients and represented one of the most frequent complaints. Postprandial fullness and/or nausea was present in twelve patients. Eructation and belching was a complaint of twelve patients. Dizziness at various times of the day but mostly in connection with the intake of food was found in eleven patients. In association with dizziness, profuse perspiration, palpitations, and increasing weakness occurred often forcing the patient to lie down after meals in order to avoid fainting. Tendency to constipation was found in eight patients, to diarrhea in two patients.

Marked signs of vitamin deficiency were present in four individuals who presented sore mouth with reddening and hypertrophy of the papillae of the tongue and in one case cheilosis. The other individuals showed only minor signs of ascorbic acid and riboflavin deficiency of the mucous membrane of the mouth as well as mild evidence of vitamin A deficiency (dry skin with hyperkeratosis and folliculitis).

It has to be mentioned that in a few of our patients additional clinical findings were present. One patient (Case 7) showed restricted motility of the left diaphragm due to a lung injury suffered during World War I. Another (Case 8) had bronchiectasis with shrinkage of the right lower lobe. One patient (Case 12) presented evidence of mild arthritis with hyperuricemia and was suspected of having gout. One patient (Case 13) had a history of malaria and evidence of mild thromboangitis obliterans. Case 14 was mentioned as a case of gastric syphilis, the patient's Wassermann reaction remained positive after intensive treatment. It is important to emphasize that the majority of these individuals presented stigmas of psychoneurosis with tendency to overemphasis and fixation of symptoms. Although some of them were inclined to attribute their "nervousness" to the poor general condition and loss of weight, psychoneurotic trends could be traced back to the period preceding the operation and the onset of the disease.

#### BLOOD MORPHOLOGY AND BLOOD PROTEINS

Morphologic blood studies failed to reveal any striking abnormality. The red blood count ranged from 3,790,000 to 5,620,000, the average being 4,436,000.



TABLE IV GASTRIC ACIDITY

NO	NAME	GASTRIC ACIDITY HIGHEST FIGURES	
		FREE ACIDITY	TOTAL ACIDITY
1	C. M.	0	14
2	G. S.	30	42
3	L. Z.	26	42
4	J. K.	0	9
5	M. C.	0	12
6	S. R.	14	26
7	S. Z.	0	14
8	R. E.	0	24
9	B. B.	0	12
10	L. R.	32	46
11	F. M.	0	15
12	R. B.	0	14
13	A. F.	16	24
14	O. S.	-	-

had to be rehospitalized. In none of the other cases was there evidence of a gastroduodenal ulcer. Special small intestine studies were performed in seven cases and failed to reveal abnormalities. A distention of the upper jejunal loops could be observed in most of the cases. There was, however, no evidence of a disturbed small intestine motility or a deficiency pattern.

In a few individuals the stools were carefully analyzed for presence of undigested food elements. Only rarely larger amounts of fatty acids and soaps, in absence of neutral fat, and occasionally undigested muscle fibers were found, while undigested starch cells did not exceed the normal limits. None of the examined patients presented frothy, bulky stools indicative of steatorrhea.

#### FASTING BLOOD SUGAR LEVELS AND GLUCOSE TOLERANCE TESTS

The fasting blood sugar was determined in all fourteen cases and was followed in thirteen patients by a glucose tolerance test with oral administration of 100 Gm of glucose. In one of the patients (Case 12) it was impossible to perform the glucose tolerance test because the administration of glucose caused, on repeated occasions, violent vomiting. It must be stated that the majority of the other patients complained of nausea and epigastric discomfort shortly after the intake of glucose and in a few instances vomiting could be prevented only by placing the patient in a horizontal position. The fasting blood sugar ranged between 70 to 146 mg per cent, the average being 101 mg per cent (see Table V). Two of the patients had a moderate elevation of the fasting blood sugar (Cases 6 and 9), in only three instances was the fasting blood sugar below 80 mg per cent, and in no instance was it lower than 70 mg per cent. The curves obtained in the sugar tolerance test were characterized by an early peak which was reached usually after one-half hour and in only three instances one and one-half hour after glucose intake. The maximum elevation ranged from 130 to 238 mg per cent, the average being 188 mg per cent. In all instances there was a rapid drop of the blood sugar after two and one-half to three and one-half hours to comparatively low figures, ranging from 51 to 80 mg per cent, the average being 60 mg per cent. The glucose tolerance test in the gastrectomized patients was thus characterized by a steep and rapid elevation of the blood sugar level with



average fasting vitamin A level of the hospital population (60 to 80  $\mu\text{g}$  per cent). The vitamin A tolerance test with 180,000 I U. of vitamin A followed the determination of the fasting level. The vitamin A serum concentration after four hours ranged from 63 to 195  $\mu\text{g}$  per cent, the average being 136  $\mu\text{g}$  per cent. Thus, the response to the vitamin A tolerance test has to be considered normal for the average patient. The character of the curve presents a normal elevation with one exception, the flat curve in Case 11.

#### COMMENT

Gastroenterologists as well as surgeons have recently become interested in the symptomatology of some gastrectomized individuals whose symptoms are not caused by a marginal ulcer and who, according to various statistics, represent 6 to 29 per cent of all patients subjected to partial gastrectomy for peptic ulcer.

A group of such patients, referred to the Nutrition Clinic of the Mount Sinai Hospital chiefly because of inability to gain weight, were subjected to a careful study. The average patient of this group had lost 15.9 pounds from the onset of ulcer symptoms to the time of the operation and, in addition, 10.1 pounds after the gastrectomy, the total loss of weight being 26 pounds. These individuals had been placed on various types of high caloric diets, supplemented by vitamin concentrates and liver extract, but failed to gain weight. Each of them presented a definite nutritional problem.

The postgastrectomy syndrome was characterized by postprandial fullness, nausea and dizziness, eructation and belching, fatigue, weakness, palpitations, perspiration, headaches, and tendency to fainting spells. A thorough analysis of these symptoms permitted a classification into early and late postprandial symptoms. The early symptoms were chiefly fullness, nausea, eructations, belching, dizziness, and tendency to vomiting, while the late symptoms occurring usually two to four hours after meals were dizziness, palpitations, perspiration, headaches, fatigue, and weakness. The early as well as the late symptoms were somewhat relieved by the assumption of a horizontal position. Because of these complaints many of the patients developed the habit of resting for various periods of time after meals. It is of interest that in many patients the late symptoms could be definitely relieved by eating while the early symptoms precluded any further food intake. The appearance of early symptoms compelled these individuals to restrict their food intake to very small amounts, the relief of late symptoms by eating taught them to take these small amounts of food at frequent intervals. One gained the impression that the early and the late postprandial symptoms were caused by different mechanisms.

Clinical observation of these individuals and a study of their case histories revealed evidence of psychoneurotic stigmas in all of them. Many of them were already stomach conscious before the operation and the shock of the operation, the immediate postoperative course with its occasional complications, the general rundown condition and malnutrition, and especially the postprandial symptoms described previously exaggerated the pre-existing stomach awareness and led gradually to a vicious circle wherein the postprandial symptoms and the fear to eat were the outstanding factors. In the extremely severe cases

the final picture may then, physically as well as psychologically, resemble that of anorexia nervosa: the patient appears underweight, there is diminished turgor of the skin, the eyes are deeply set, he is morose, self-centered, and full of anxiety and hypochondriac ideas centering about the stomach. The basal metabolic rate may be low, as exemplified by the patient (Case 4) whose basal metabolic rate ranged between -11 to -19 per cent.

The morphologic blood picture was practically normal with an occasional tendency to hypochromic microcytic anemia. Berkman and Heck<sup>2</sup> and others have found this type of anemia more frequently among their gastrectomized patients, while Farris, Ransom, and Coller<sup>3</sup> encountered it, as we did, only occasionally. The blood proteins as well as the partition were normal with one exception. There were only mild signs of nutritional deficiency consisting of smoothness and reddening of the tongue. In the latter cases there was moderate hypertrophy of the papillae, occasional cheilosis, moderate hyperkeratosis, and folliculitis of the skin.

Röntgen studies of the gastrointestinal tract failed to reveal any abnormality in the function of the stomach or of the small intestine. The majority showed rapid evacuation of the gastric stump with the usual subsequent overfilling of upper jejunal loops. One patient developed a marginal ulcer in the later course.

The fasting blood sugar averaged 101 mg per cent. Only in three cases was the fasting blood sugar below 80 mg per cent and in no instances lower than 70 mg. per cent. There was no evidence of hypoglycemia or hypoglycemic symptoms in the fasting state. The glucose tolerance curve showed usually rapid and steep elevation up to 258 mg per cent, with an average level of 188 mg per cent, and a rapid steep drop to an average of 60 mg per cent two and one-half to three and one-half hours after the glucose test meal. In the course of the test a considerable number of individuals eliminated glucose in the urine in concentrations ranging from 0.9 to 7.5 Gm per cent. Since none of these patients had diabetes, the extent of the glycosuria was remarkable and had to be attributed to the rapid absorption of sugar from the intestinal wall and the transient elevation of the blood sugar level over the normal kidney threshold for glucose. The possibility, however, of a pancreatic origin of some of the high blood sugar curves in connection with a pre-existing penetrating duodenal ulcer and a probable injury to the pancreas cannot be excluded.

The question arises whether any relationship exists between the pattern of the glucose tolerance test and the patient's symptoms. Glaessner<sup>4</sup> attributed the early postprandial symptoms to a hyperglycemic shock. We are inclined to doubt the importance of hyperglycemia in this connection since there is no other instance known in which hyperglycemia would lead to similar symptoms of shock. We would rather attribute the early phase of postprandial symptoms to mechanical factors: the small stomach, the rapid emptying of the stump, the rapid filling and distention of the jejunum, and the subsequent mesenteric irritation. The late postprandial symptoms, however, are in all probability closely related to chemical factors and to the rapid and steep decrease of the blood sugar level. In their clinical manifestations the late symptoms resemble the typical state of hypoglycemia and are relieved by food intake. Interestingly enough, the symptoms of these patients can be reproduced experimentally by the glucose



tolerance test in the early stage of the test epigastric pressure, fullness, nausea, and occasional vomiting are encountered; in the late stage of the test, palpitations, headaches, dizziness, and perspiration occur. One has to consider, however, that symptoms of hypoglycemia are not infrequently encountered in ulcer patients not operated upon and occasionally in apparently normal individuals. Evensen<sup>10</sup> found hypoglycemic symptoms in 30 per cent of his patients with gastroenterostomy, in about 15 per cent of patients with resected stomachs, in 8 per cent of patients suffering from peptic ulcer not operated upon, and in 6 per cent of normal individuals. Glucose deficiency has been considered to be the cause of fatigue and weakness by many authors (Wilder,<sup>11</sup> Gillespie,<sup>12</sup> Portis and Zitman,<sup>13</sup> Alexander and Portis,<sup>14</sup> and Karlan and Cohn<sup>15</sup>).

In the light of these findings the mechanism of the postprandial symptoms may be explained as follows: after the intake of food there occurs rapid filling and distention of the small stomach, rapid emptying of the stomach stump, and overflowing of the jejunum, causing rapid absorption of carbohydrates and steep elevation of the blood sugar level. In this stage the symptoms are probably due to mechanical factors (and in some cases possibly to the absorption of unchanged proteins with the subsequent effect of shock). The posthyperglycemic hypoglycemia is probably the chemical cause of the late symptoms. This tendency to hypoglycemia in these patients is probably caused by a multiplicity of factors. The rapid and early elevation of the blood sugar level per se (caused by the rapid emptying of the stomach) is probably one of them since it is known that there exists a reciprocal relationship between the height of the hyperglycemic rise and the depth of the later hypoglycemic phase. The tendency of ulcer patients who were not operated upon to hypoglycemia may be another factor. Whether or not the ulcer patient develops this occasional disturbance of carbohydrate regulation on the basis of some central neurogenic or psychogenic factors cannot be discussed here. While Alexander and Portis<sup>14</sup> are of the opinion that emotional factors are responsible for hypoglycemia via the vagus nerve, Karlan and Cohn<sup>15</sup> found that the state could not be blocked by atropine.

There is another factor that must be taken into consideration. It is known that the preceding diet affects the character of the glucose tolerance test: high carbohydrate, low fat diet flattens, while low carbohydrate high fat diet raises the glucose tolerance curve. Ulcer diets are, as a rule, high fat diets and their use prior to the test may be another factor responsible for the blood sugar pattern.

The examination of the vitamin A serum concentration and vitamin A tolerance tests revealed, as a rule, normal figures, in only one instance a flat curve was encountered, resembling the vitamin A tolerance curves found in sprue.<sup>16</sup> Occasionally, larger amounts of unabsorbed fatty acids and soaps and moderate amounts of undigested muscle fibers were found in the stools, while evidence of a disturbed starch absorption was not present. In not a single case, however, did the stools resemble the frothy, bulky, light-colored stools of sprue.

Flat glucose tolerance curves are occasionally found following gastric resection. We observed it in three gastrectomized patients who could not be included in this study. These findings may indicate that in some individuals dis-

turbed intestinal absorption is a factor, which should not be overlooked and which certainly deserves further study (see Wollaeger, Comfort, Weir, and Osterberg<sup>17</sup>).

#### SUMMARY

1. A group of fourteen patients, who for many years after partial gastrectomy for ulcer had been unable to gain weight and presented difficult nutritional problems, have been investigated. The symptoms were analyzed and divided in two groups: early and late postprandial symptoms.

2. The early symptoms were caused by mechanical factors, small stomach and rapid emptying, and overflowing of the small intestine. The late symptoms were due to chemical factors, hypoglycemia secondary to the exaggerated postprandial hyperglycemia, and occasionally secondary to disturbed intestinal absorption.

3. The postgastrectomy syndrome was caused by a sequence of these early mechanical and late chemical factors, exaggerated by distinct psychoneurotic stigmas. Many of these individuals were stomach conscious. The shock of the operation, the postoperative course, later the postgastrectomy symptoms, and finally the diminished physical and mental resistance associated with underweight and malnutrition exaggerated the stomach awareness. The ultimate effect was a conflict between the postprandial symptoms, the late manifestations of which are relieved by food, and the fear to eat. The treatment of these patients presents a series of difficult clinical, nutritional and psychologic problems, all of which require consideration.

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## THREE HUNDRED SEVENTY-FOUR ACUTE WAR WOUNDS OF THE THORAX

CHARLES B. BEEBANK, M.D.,\* BOSTON, MASS., WILLIAM H. FAIRER, M.D.,\*  
AKRON, OHIO, AND HOWARD W. JONES, JR., M.D.,\* BALTIMORE, MD.

THIS paper presents the experience of a number of teams of the Fifth Auxiliary Surgical Group in the treatment of 374 intrathoracic wounds in the European Theatre of Operations from Sept. 16, 1914, to May 15, 1915. Combined wounds of the thorax and abdomen are not included, as they are reported elsewhere.<sup>1</sup>

Two hundred and eighty-three individuals were treated in Field Hospitals with an average time between injury and operation of about seven hours. The remaining ninety-one were taken to Evacuation Hospitals with an average time between injury and operation of ten hours.

*Preoperative Care*—Patients were admitted directly to the hospital shock ward and there prepared for operation. The treatment of individuals with penetrating or perforating wounds of the thorax was complicated not only by severe shock but by certain special problems associated with thoracic injuries. The treatment of shock differed little from that employed for wounds elsewhere in the body and will not be recounted. Reference may be made to other papers for details.<sup>2</sup> The special problems involved in the preoperative treatment of casualties with thoracic wounds will be considered at length.

The incidence of injury according to the standard method of wound classification is given in Table I.

The principal emphasis in the treatment of sucking wounds has been placed on immediate closure as a lifesaving measure. For present statistical purposes every wound has been considered as a sucking wound if (1) it was reported as sucking on the Emergency Medical Tag previous to reception in the hospital, whether or not it was sucking when the dressing was removed, and if (2) it was sucking spontaneously in the hospital.

Although no one can deny the urgency of closing a sucking wound, once it is sealed by petrolatum gauze no priority for definitive care need be given. This is borne out by reference to Table II in which the same mortality for both the sucking and nonsucking groups of cases is shown.

Hemothorax occurred in 79 per cent of the cases. In the 289 cases in which it was present there were up to 2,500 c.c. of blood. The preoperative treatment was and should be conservative. A small collection of blood, 200 to 300 c.c., in the absence of other factors, was left alone. If respiratory embarrassment dictated aspiration before definitive care could be instituted, aspiration with a large needle was done. If hemothorax rapidly recurred, high priority was given for an immediate operative procedure. At the time of

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\*Formerly Major, Medical Corps, Army of the United States.

TABLE I. WOUND STATISTICS—774 PATIENTS

Causative agent	Gunshot wounds	193
	Shell fragment wounds	181
Location	Left	180
	Right	189
	Bilateral	5
Type	Penetrating	213
	Sucking	120
	Non-sucking	93
	Perforating	161
	Sucking	61
	Non-sucking	100

aspiration no air was reaspirated into the pleural cavity. An intrapleural injection of 40,000 units of penicillin routinely followed aspiration.

In some instances where a thoracotomy was not indicated and the wound did not require débridement as with perforating gunshot wounds, aspiration of the hemothorax constituted the principal method of therapy.

Pneumothorax per se was not treated in the preoperative ward unless respiratory embarrassment was present. Under this circumstance there was no hesitancy in doing a simple aspiration.

TABLE II. COMPARISON OF SUCKING AND NONSUCKING WOUNDS

SUCKING			NONSUCKING		
NUMBER OF CASES	DEATHS	MORTALITY (PER CENT)	NUMBER OF CASES	DEATHS	MORTALITY (PER CENT)
181	15	8.3	194	16	8.3

Tension pneumothorax was an unusual preoperative complication occurring but thirty-two times. In the majority of cases it was due to a valvelike type of sucking wound and in the remainder to a punctured lung. Although the former type of injury could be treated by sealing the wound and aspiration, the uncertainties of diagnosis required the introduction of a large needle or a stiff catheter into the second intercostal space anteriorly. This was attached to a drainage apparatus with water seal.

*Anesthesia*—In thoracic casualties anesthesia was of great importance. In the presence of a sucking wound or an intrathoracic procedure, endotracheal gas, oxygen, and ether was the anesthetic of choice. A preliminary induction with pentothal sodium was frequently used. This obviated a period of excitement which might reopen a temporarily sealed sucking wound or start fresh bleeding from the lung. Either of these complications made the further administration of anesthesia very difficult and hazardous.

The advantage of being able to use positive pressure for expanding the lung and to stabilize the mediastinum during intrathoracic surgery is so great that further justification of endotracheal anesthesia is unnecessary. The various kinds of anesthetics used are shown in Table III. Among the 281 endotracheal anesthetics there were twenty-six deaths, a mortality of 9 per cent. None of these were considered directly attributable to the anesthetic.

TABLE III TYPE OF ANESTHETIC EMPLOYED

ANESTHETIC	IN ALL WOUNDS		IN SUCKING WOUNDS	
	NUMBER OF CASES	PER CENT	NUMBER OF CASES	PER CENT
Endotracheal gas oxygen ether	261	75	110	78
Local	83	22	27	14
Pentothal sodium	6	2	5	3
Gas-oxygen	4	1	9	5

*Operative Management of Thoracic Wounds*—The criteria for the operative treatment of intrathoracic wounds changed during the campaign in Western Europe. In the beginning, the general tendency was towards the radical view and consequently there were few patients who did not undergo thoracotomy. It was found, however, at busy times when abdominal and thoracoabdominal wounds were considered to have a high priority, that some chest wounds could be cared for by less radical procedures. This led to the formation of the following definite indications for thoracotomy.

1 Hemothorax due to active bleeding. These patients were usually in severe shock on admission and did not respond well to shock therapy. The source of bleeding was either an intercostal or internal mammary vessel, the lung, or more rarely the heart or mediastinal structures (Table IV).

TABLE IV ACTIVE INTRATHORACIC HEMORRHAGE DEMONSTRATED AT OPERATION IN FIFTY CASES

	NUMBER OF CASES	PER CENT
Source		
Lung	33*	66
Intercostal vessel	16	32
Internal mammary vessel	2	4
Causative agent		
Shell fragment	32	64
Gunshot	18	36

\*One case combined hemorrhage both from lung and intercostal vessel

2 Hemothorax which could not be aspirated, usually due to clotted blood. These patients often showed dyspnea, cyanosis, and mediastinal shift. Under these circumstances an open thoracotomy was undertaken to prevent organization of the blood and the possible necessity for a decortication of the lung at a later date.

3 The presence of a foreign body 2 cm or larger in the lung parenchyma or pleural cavity. Such particles were removed to obviate the danger of lung abscess or infected hemothorax.

4 The presence of shattered rib fragments either in the lung or pleural cavity or large fragments which had not perforated the pleura. These indicated thoracotomy or extrapleural rib resection. It should be added that many surgeons came to feel that bone fragments in the lung were of more serious consequence than metallic foreign bodies.

5. Tension pneumothorax due to a bronchopleural fistula required thoracotomy for lung suture.

A sucking wound was not considered an indication for a thoracotomy. Débridement and closure were performed unless one of the previously mentioned indications for thoracotomy was present also. With these indications for thoracotomy, treatment was in general more conservative. However, it was observed that the more radically treated patients often had smoother post-operative courses. Temperature and pulse elevations were less as a result of the operative removal of all serum and blood, both liquid and clotted. Post-operation serum collections were readily aspirated so that a high percentage of individuals could be evacuated with a dry pleural cavity and completely re-expanded lung. Furthermore, reports from general hospitals indicated that in those patients treated conservatively the incidence of empyema, lung abscess, and infected hemothorax was greater than in those treated radically. This was especially true in the presence of small foreign bodies. Finally, directives from the surgeons office stated that all foreign bodies of whatever size should be removed because of the high incidence of late lung abscess and empyema.

Thus, toward the end of the War in Europe foreign bodies of a size large enough to find and suspected lung lacerations especially from shell fragment wounds were added to the indications for thoracotomy. In spite of the wider indications for thoracotomy, the majority of cases did not require this procedure.

In sixty-five instances, comprising mainly perforating gunshot wounds, a dry dressing was the only treatment necessary for the wound.

In 167 cases a débridement was the only procedure carried out. This included both sucking and nonsucking wounds and many times resulted in the conversion of a nonsucking wound to a sucking one. It was therefore often an arbitrary decision as to whether a given case should be classified as an extensive débridement or a thoracotomy through the wound.

In thirty-two instances a trocar thoracotomy with the establishment of tube drainage was added to one of the previously mentioned procedures, and it is our opinion that this procedure might have been used more often.

In 142 incidences, or 38 per cent of the cases, a formal thoracotomy was done. Operative procedures varied according to the pathology. Lacerations of the lung were sutured, foreign bodies removed, rib fragments excised, blood and clot evacuated. One pneumonectomy was performed for severe laceration of both the upper and lower lobes, convalescence was uneventful. In another instance a large laceration was sutured, and on re-expansion of the lung with positive pressure there was a massive intrabronchial hemorrhage resulting in death of the patient. In retrospect a lobectomy should have been performed on this patient. The indications for such radical surgery, however, were rare.

The location of the incision was seldom troublesome; in most instances it was made at the wound of entrance. If there was extensive rib damage entrance was made through the bed of a resected rib; if little or no rib damage was present an intercostal incision was made. When there was reason to have access to a part of the chest not readily available through an enlargement of the wound, no hesitancy was felt in doing a simple débridement and closure followed by a thoracotomy through an incision that would give access to the

desired area. For example, there was a case in which a bullet entered the upper right chest and finally lodged in the lower lobe of the right lung; the wound of entrance was closed and a formal intercostal thoracotomy performed at the optimum level both for the removal of the foreign body and the examination of the entire right lung.

A sucking wound at the apex of the lung anteriorly commanded special attention as it could easily be mistaken for a perforation of the trachea. Approach to this area was difficult but could be accomplished by a division of the clavicle and elevation of the fragments.

A perforating wound of the wing of the scapula was also troublesome as it was frequently difficult to evaluate the extent of injury to the chest wall. The most satisfactory operation could be done by elevating the scapula through a thoracoplasty incision. Many times a wound which was not sucking exteriorly was found to do so as the scapula was elevated.

Thoracotomy incisions were closed with pericostal silk or wire sutures and the soft tissues with catgut. Following débridement small wounds were closed in layers with catgut.

Regardless of the procedure required by the wound itself, the aspiration of blood from the pleural cavity was considered a necessary part of the definitive care. Many times this was done with an aspirating needle. It was not considered necessary to remove the entire amount at one sitting and frequent postoperative aspirations were the rule.

The question of tube drainage was perplexing and debated. Difference of opinion arose not so much concerning the desirability of the procedure which was conceded but because of the lack of constant and meticulous postoperative care so necessary to the satisfactory operation of the water-seal drainage. For this reason the number of drainage tubes was less than would be required under more ideal circumstances. If tube drainage was used a No. 26 or 30 rubber catheter or tube was employed. The tip with numerous holes was sutured high on the anterior parietal wall. Sometimes constant suction was attached to help remove the fluid and re-expand the lung.

Following major procedures bronchoscopic aspiration was frequently used on the operating table.

In the 142 major procedures (almost all thoracotomies) there were twelve deaths, a mortality of 8.4 per cent. In the remaining 232 cases there were nineteen deaths, a mortality of 8.2 per cent.

**Heart Injuries.**—There were four individuals with injuries to the heart muscle.

**CASE 1.**—There was a small laceration of the left ventricle. The wound of entry was sucking through the left fifth interspace. Through an anterior approach the laceration was sutured with fine silk and the pericardium loosely closed. Recovery was uneventful.

**CASE 2.**—There was a sucking wound of entrance through the right fourth rib. A shell fragment had passed through the lower lobe and out posteriorly. There was a laceration of the right atrium and of the right phrenic nerve. The perforating wound of the lower lobe of the right lung was repaired and the heart laceration was sutured with fine silk. The pericardium was loosely closed and the chest was drained. Recovery was uneventful.

CASE 3.—There was a penetrating sucking wound in the left seventh interspace in the anterior axillary line. In addition there were multiple penetrating wounds of the back and thighs. A débridement and closure of the chest wound was done. The patient died suddenly on the operating table. Autopsy revealed a shell fragment lodged in the wall of the left ventricle having lacerated the ramus descendens of the left coronary artery. A foreign body had been noted in the anteroposterior chest plate but was thought to be in the mediastinum.

CASE 4.—There was a penetrating chest wound similar to that in Case 3. The wound of entrance was in the right upper chest. By x ray there was a foreign body lying in the center of the heart shadow, and in the lateral view it was thought to be in the posterior mediastinum. At thoracotomy a laceration of the right upper lobe was found but the patient died suddenly on the operating table. Autopsy revealed a shell fragment 25 by 15 by 10 mm in the right ventricle. The foreign body had entered the superior vena cava, passed through the auricle, and perforated the tricuspid valve as it entered the ventricle.

*Bilateral Thoracic Wounds*—There were five patients with bilateral intra-thoracic injury, two of whom died.

CASE 1.—There were bilateral perforating wounds of the chest and both wounds of exit were sucking. The patient was critically ill. All wounds were débrided and closed under local anesthesia. After doing well for seven days the patient suddenly died. An autopsy revealed a secondary hemorrhage from a laceratedazygos vein.

CASE 2.—This patient was wounded by one bullet which entered the right chest anteriorly and left through the left chest posteriorly. Neither wound was sucking, and débridement and closure were done under local anesthesia. Recovery was uneventful.

CASE 3.—In this case the bullet passed through both chests from right to left superiorly. Bilateral thoracotomies were performed. This is the only case of such a combined operation recorded in the series. The left upper lobe only was injured. The postoperative course was satisfactory.

CASE 4.—In this case a bullet entered through the right chest and penetrated into the left. The wound of entry was sucking and was débrided and closed. A thoracotomy was performed on the left side and the foreign body removed. Recovery was uneventful.

CASE 5.—There was a perforating wound caused by a missile proceeding from right to left. The sternum was fractured and depressed, and there were bilateral sucking wounds. The sternum was elevated with constant traction, and the wounds were closed. The patient developed bilateral pneumothorax which could not be controlled by continuous aspiration and died of anoxia on the third day.

In addition to the myocardial injuries there were three lacerations of the pericardium without myocardial damage. These lesions were sutured without mishap. One patient died from a complicating skull injury.

*Esophageal Wounds*—There were three patients with wounds of the thoracic esophagus. Each wound was sutured with catgut. All recovered.

*Postoperative Care*—Thoracic wounds require certain special postoperative procedures in addition to intravenous blood and plasma to combat shock, morphine for pain, penicillin, and sulfadiazine. Many patients had tube drainage and constant care was required to keep the water-seal drainage system in operating order. From time to time cases were discovered with drainage tubes open to the air. Fortunately no death was attributed to this cause.



In cases without the tube drainage, and in some with, it was routine to aspirate with needle and syringe any accumulation of intrathoracic fluid. This was done daily or more often if necessary. It was routine to inject 40,000 units of penicillin into the pleural cavity after each aspiration. It was attempted to evacuate patients from the fifth to tenth postoperative day with a dry thoracic cavity.

Unless pressing circumstances prevailed all thoracic wounds had bronchoscopic aspiration before leaving the operation table. Bronchial obstruction was often troublesome and daily or more frequent aspiration was lifesaving in some cases.

A Levine tube with suction was routine for forty-eight hours to prevent gastric dilatation.

Oxygen via B.L.B. masks was used when necessary.

**Mortality**—In the 374 cases there were thirty-one deaths, a mortality rate of 8.2 per cent.

The types of wounds encountered in the fatal cases are shown in Table V. There were ten major thoracotomies, nineteen débridements and simple closures, one anterior mediastinotomy, and the elevation of one compound fracture of the sternum.

TABLE V. WOUND STATISTICS IN THIRTY ONE FATAL CASES

Causative agent		
Gunshot wounds		6
Shell fragment wounds		25
Location		
Left		15
Right		14
Bilateral		2
Type		
Penetrating		16
Sucking	10	
Nonsucking	6	
Perforating		15
Sucking	5	
Nonsucking	10	

Hemothorax was present in all thirty-one fatal cases in amounts varying from 200 to 2,500 cubic centimeters. The increase in mortality with the amount of hemothorax is demonstrated in Table VI.

An attempt is made in Table VII to correlate mortality with severity of injury.

The causes of death are given in Table VIII. Case 5 in Table VIII was interesting enough to deserve special notes. This patient had a penetrating

TABLE VI. RELATION OF VOLUME OF HEMOTHORAX TO MORTALITY

VOLUME OF HEMOTHORAX (C.C.)	NUMBER OF CASES	DEATHS	MORTALITY (PER CENT)
0 to 500	49	2	4
500 to 1,000	53	3	5.6
1,000 to 1,500	41	5	12
1,500 to 2,000	68	9	13
2,000 to 2,500	73	12	15.4

TABLE VII. EFFECT ON MORTALITY OF INCREASE IN NUMBER OF MAJOR INJURIES

TYPE OF INJURY	NUMBER OF CASES	DEATHS	MORTALITY (PER CENT)
No visceral injury (pulmonary or other) and no major extrathoracic injury	178	4	2.2
One visceral injury	88	7	7.9
Two visceral injuries	13	4	30.0
Three or more visceral injuries	4	2	50.0
Visceral injury without major extrathoracic injury	48	5	10.0
Visceral injury with major extrathoracic injury	43	9	20.0

TABLE VIII. CAUSE OF DEATH

CASE	TIME INTERVAL BETWEEN OPERATION AND DEATH	CAUSE OF DEATH
1	3 hr	Blast injury to both lungs
2	7 days	Pneumonia both lungs
3	7 days	Delayed hemorrhage from lacerated axillary vein
4	1 day	Blast injury to both lungs
5	3 days	Fibrinous pleuritis
6	8 hr.	Blast injury to lungs
7	1 day	Unknown
8	7 days	Meningitis—patient had cord transection
9	7 days	Severe contusion of lung
10	3 days	Shock
11	Died at operation	Unknown
12	2 hr.	Blast injury to lungs
13	Died at operation	Vagovagal reflex—patient had mediastinotomy
14	1 hr.	Shock—patient bled from lacerated axillary vein
15	7 days	Pneumonia both lungs
16	15 min.	Shock
17	1 hr.	Shock
18	7 hr.	Shock
19	4 days	Crushed lung
20	Died on table	Shock
21	Died on table	Lacerated ventricle
22	Died on table	Intrabronchial hemorrhage
23	1 day	Shock
24	1 day	Compound skull fracture
25	12 hr.	Shock
26	12 hr.	Shock
27	Died on table	Lacerated right ventricle and superior vena cava
28	3 days	Anoxia
29	2 hr.	Shock
30	1 hr.	Shock
31	1 day	Shock

TABLE IX. TIME OF DEATH IN RELATION TO OPERATION

TIME INTERVAL BETWEEN OPERATION AND DEATH	NUMBER OF CASES	MORTALITY (PER CENT)
Died at operation	6	19.3
Zero to twelve hours postoperative	10	72.2
Twelve to twenty four hours postoperative	6	19.3
Second day postoperative	0	0
Third day postoperative	3	9.4
Fourth day postoperative	1	3.6
Fifth day postoperative	0	0
Sixth day postoperative	0	0
Seventh day postoperative	5	16.2
Totals	31	100.0

sucking wound of the left chest. By x-ray the stomach was shown to be high. However, the patient stated that as a boy he had had a left phrenicectomy for tuberculosis. It was the feeling of the surgeon that the diaphragm was elevated due to the old phrenic crush and that the stomach was below the diaphragm. A débridement and closure of the chest wall wound were done. Postoperatively the patient did poorly and died on the third day. Autopsy revealed a congenital diaphragmatic hernia of the stomach which has been perforated.

Shown in Table IX is the relation of mortality to the interval between operation and death. It will be seen that sixteen patients, or 52 per cent of the cases, died in the first twelve-hour period; of these, ten deaths, or 62 per cent, were attributable to shock. Additional analysis reveals that 71 per cent of those patients who died in the first twenty-four hour period died of shock.

#### SUMMARY

A series of 374 intrathoracic war wounds with a gross mortality of 82 per cent has been presented. The special problems associated with preoperative management of thoracic wounds have been outlined, the operative management considered, and the postoperative care detailed. Finally, the fatal cases have been analyzed from several points of view. Shock proved to be responsible for the majority of fatalities.

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## THE SIX SUBPHRENIC SPACES

### APPLIED ANATOMY AND SURGICAL CONSIDERATIONS

PHILIP THOREK, M D

CHICAGO, ILL

(From The Department of Surgery, University of Illinois, The American and Cook County Hospitals, and The Cook County Graduate School of Medicine)

THIS paper has been titled "The Six Subphrenic Spaces" to emphasize the importance and existence of six distinct anatomic spaces in this region. This, in turn, aids in earlier recognition and treatment of subphrenic infections and abscesses. There are many ways of describing the anatomy of the subphrenic region, but the description must be kept both anatomic and practical.

The frequency of subphrenic involvement was emphasized in a rather exhaustive study by Ochsner and Graves' in 1933. They reported and analysed 3,372 cases collected from the literature and their personal cases. If the presence of subphrenic pathology be kept in mind, especially as a complication of intra-abdominal suppurative processes, it can be diagnosed earlier and treated more effectively.

*Anatomy*—Martinent,<sup>2</sup> as far back as 1898, accurately described the subphrenic spaces. In 1908, Barnard<sup>3</sup> amplified this description and included the surgical aspects. These studies will be utilized and somewhat modified in the hope that a clear-cut picture of the six anatomic spaces will result.

The subphrenic space per se must be looked upon as that space which exists between the diaphragm above and the transverse colon and its mesocolon below. This area is divided by the liver into supra- and infrahepatic portions. The suprahepatic part is bounded above by the diaphragm and below by the upper surface of the liver. The infrahepatic part is bounded above by the undersurface of the liver and below by the transverse colon and its mesocolon. Three suprahepatic and three infrahepatic spaces exist (Fig. 1). The falciform ligament divides the suprahepatic area into right and left parts. To understand the nomenclature and construction of these spaces, the anatomy of the liver should be reviewed. This can best be done by visualizing cross sections of the right and left lobes of the liver, thereby differentiating the superior from the inferior surfaces of this organ. The superior surface of the right lobe of the liver resembles an inverted cup or bowl, so that this surface appears both anteriorly and posteriorly. The cut section of the left lobe, however, resembles a chip so that the dome-shaped anterior and posterior relations of the superior surface are wanting. On the right side, the right lateral ligament which is a prolongation of the coronary ligament divides this area into two spaces, a large anterior and a small posterior one. These ligaments are peritoneal reflections. The left lateral ligament passes along the posterior border of the left lobe of the

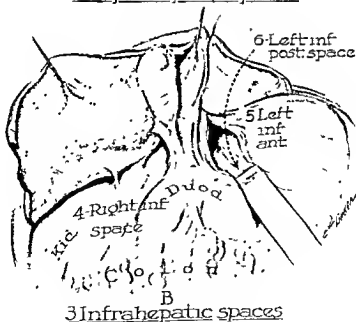
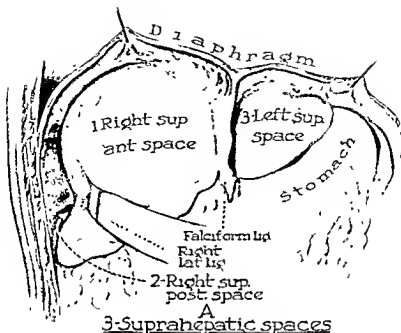


FIG 1 (For legend see opposite page)

liver and separates the superior from the inferior surface. Therefore, only one space exists to the left of the falciform ligament. The three suprahepatic spaces thus constructed are named in the following way (Fig 1, A): 1, the space which exists above the liver, anterior to the right lateral ligament and to the right of the falciform ligament, is called the right superior anterior subphrenic space. Space 2 is located to the right of the falciform ligament, takes in the superior surface of the liver, and is behind the right lateral ligament, therefore, it is called the right superior posterior subphrenic space. Space 3 is situated between the liver and the left half of the diaphragm and hence, is known as the left superior subphrenic space.

The infrahepatic area (Fig 1, B) is conveniently divided into right and left parts by the descending portion of the duodenum, although some anatomists use the ductus venosus for this division. To the right of the duodenum and below the liver, the right inferior subphrenic space is located, which is the same as the hepatorenocolic pouch of Morrison. The left side of the infrahepatic space is divided by the stomach into anterior and posterior parts. This creates a space which exists to the left of the duodenum and in front of the stomach and hence, is named the left inferior anterior subphrenic space. This also has been referred to as the perigastric space. The final, or sixth space, is situated to the left of the duodenum, below the liver but behind the stomach, it is known as the left inferior posterior space or the lesser peritoneal cavity (omental bursa).

The six spaces are all intraperitoneal, but an extraperitoneal space exists within the confines of the coronary ligament which corresponds to the bare area of the liver. It separates the right superior posterior from the right superior anterior space and is of little clinical importance. Unfortunately, the space most frequently involved is the one which is smallest and most difficult to reach, namely, the right superior posterior. This is due to the fact that the most frequent causes of subphrenic infection are on the right side, namely, acute appendicitis, acute cholecystitis, and perforated peptic ulcer. An inflammatory exudate from any of these three lesions may travel upward along the so-called paracolic groove of the ascending colon and localize in this space, which is the most difficult to reach surgically and the most difficult to diagnose.

The microorganisms most commonly responsible for subphrenic infection or abscesses are the colon bacillus, staphylococcus, and streptococcus. Usually a mixed infection is present. These organisms can gain entrance intraperi-

FIG 1—A. The three suprahepatic spaces. The suprahepatic region is divided by the falciform ligament into right and left parts. Space 1 is situated to the right of the falciform ligament, above the liver and anterior to the right lateral ligament. It is therefore, called the right superior anterior space. Space 2 is located to the right of the falciform ligament, above the liver and behind the right lateral ligament. It is called the right superior posterior space. Spaces 1 and 2 are separated from each other posteriorly by the bare area of the liver (see Fig 2, B). Space 3 is found to the left of the falciform ligament and since the left lateral ligament passes posteriorly along the flattened left lobe of the liver, there is only one space on this side in contrast to the two on the right. It is called the left superior space.

B. The three infrahepatic spaces. The infrahepatic region is divided by the descending duodenum into right and left parts. For convenience we have numbered these spaces 4, 5, and 6. Space 4 is to the right of the duodenum and below the liver. It is, therefore, called the right inferior space. This is the same as the hepatorenocolic pouch of Morrison. Space 5 is found to the left of the duodenum, below the liver and in front of the stomach. It is called the left inferior anterior space. Space 6 is located to the left of the duodenum, below the liver and behind the stomach. It is called the left inferior posterior space or lesser peritoneal cavity. The arrow indicates its position and surgical approach.

toneally or through vascular channels. Less frequently, however, lesions in the thorax may pass through the diaphragm and into the subphrenic spaces. Intrathoracic involvements are usually complications rather than causes of subphrenic infection. Therefore, a little fluid or involvement of the thorax may mask the clinical picture of the subphrenic pathology and the patient is incorrectly treated for an intrathoracic lesion. Dexter<sup>4</sup> has emphasized the importance of draining a subphrenic abscess before the structures above the diaphragm become involved. This would have a tendency to keep the mortality and morbidity low. Other intrathoracic complications which may make the diagnosis difficult are bronchopleural fistula, lung abscess, and pneumonitis.

All subphrenic infections do not result in subphrenic abscesses. In their analysis, Ochsner and Graves<sup>1</sup> concluded that approximately 30 per cent of subphrenic infections proceeded to suppuration and the remaining 70 per cent subsided spontaneously. It becomes important, therefore, to differentiate diagnostically the nonsuppurative involvement from the true abscess since the therapy of each is different. Almost all subphrenic infections respond to conservative therapy, especially since the advent of modern chemotherapy. This type of treatment, however, will not cure a subphrenic abscess which needs the proper institution of evacuation and drainage.

The diagnosis of subphrenic abscess can usually be made if the condition is kept in mind. The inaccessibility of the subphrenic region also accounts for the delay in diagnosis, but there are many signs and symptoms which will suggest the possibility of this lesion. The onset may be abrupt or insidious, but the one outstanding finding is continuous fever. An unexplained fever which persists following a suppurative intraperitoneal process should at least suggest subphrenic abscess. The patient complains of pain or a sense of pressure in the upper abdomen or loin, which is usually aggravated by deep inspiration and thus may be confused with pleurisy or pneumonia. If an infection is present in the right posterior superior space, the pain may be referred to the lumbar region; however, those cases which involve the right anterior superior space or right inferior space usually have pain which is referred to the right costal margin. Localized tenderness which is found over the involved region is of greatest diagnostic importance, however, its absence does not rule out subphrenic pathology. If an abscess is present in the right posterior superior space, the tenderness localizes over the right twelfth rib. By the same token, local tenderness is found along the costal margin, on their respective sides, in right anterior superior, right inferior, left superior, and

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Fig. 2—A, Diagrammatic figure to show the skin incision placed over and parallel with the twelfth rib and the deeper transverse incision at the level of the first lumbar spinous process. If this change in position of incisions is kept in mind, the pleural cavity will not be entered.

B, The retroperitoneal approach to an abscess in the right superior posterior subphrenic space. The twelfth rib has been removed and the incision deepened to the peritoneum, the finger peels the peritoneum from the undersurface of the diaphragm until the abscess is entered. This approach avoids both pleural and peritoneal cavities.

C, Incision for drainage of an abscess in the right superior anterior subphrenic space. It is placed below and parallel with the right costal margin and is continued to but not through the peritoneum.

D, Approach to a right superior anterior subphrenic space. The finger peels the parietal peritoneum from the undersurface of the diaphragm until the abscess cavity is entered. In this way extraperitoneal drainage is instituted.

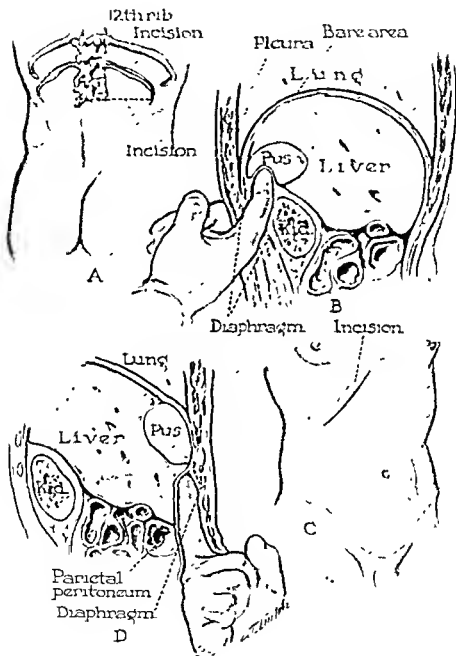


Fig. 2 (For legend see opposite page.)



left anterior inferior space abscesses. The liver is displaced downward and an area of increased liver dullness to percussion will be found in involvement of the right anterior superior, right posterior superior, and left superior space abscesses. The x-ray is of great help if one emphasizes the importance of the fluoroscope instead of the x-ray plate. Although it is true that the diaphragm is elevated in subphrenic abscess, this in itself is not pathognomonic. On the other hand, immobility of the hemidiaphragm on the involved side is most suggestive of subphrenic pathology, this sign is of utmost importance and is most essential to the diagnosis. The presence of gas represents a late finding hence, a neglected case, however, its absence, denoting a more favorable condition, does not eliminate the diagnosis of subphrenic abscess.

The use of aspiration in the diagnosis is feared because of the danger of contaminating the pleural or peritoneal cavities. Many enthusiasts of this method emphasize the fact that this procedure should only be done immediately before operation so that if pus is found, immediate incision and drainage may be instituted, however, we do not share this view.

The treatment is dependent upon the location of the infection and the presence or absence of suppuration. Since the majority of subphrenic infections do not go on to suppuration, these may be treated by conservative measures, especially making use of modern chemotherapy. The clinical course of such a case is carefully watched and charted, if there is no improvement and the white blood count goes over 20,000, this is most suggestive of a suppurative process which will necessitate surgical intervention and drainage. It is of utmost importance to avoid contaminating uninvolved cavities in the drainage of such an abscess. This is imperative where the pleural and peritoneal cavities are concerned, since the marked absorbability of serous membranes might produce an immediate overwhelming toxemia. Ochsner and Graves<sup>1</sup> have divided the surgical approach into either transthoracic or transabdominal, which in turn are divided into transserous and extraserous. The transthoracic extraserous approach can be accomplished by incising below the reflection of the pleura or by mobilizing the costophrenic angle of the pleura upward. The transabdominal extraserous approach (Fig 2, C and D) may be accomplished by incising directly over the abscess, if the abscess is extraperitoneally placed, or by mobilizing the parietal peritoneum from the undersurface of the diaphragm and following this to a suprahepatic abscess. If an intraperitoneal abscess exists, in which adhesions between the parietal peritoneum and the abscess are present, the cavity may be drained "extraserously" since the incision is made through the adhesions and the peritoneal cavity remains uncontaminated. The ideal procedure, therefore, is an extraperitoneal one approaching the abscess either from in front or from behind, depending upon the location of the abscess. Since the right superior posterior space is the one most frequently involved, a "retroperitoneal operation" is usually performed (Fig 2, A and B). This procedure has been too frequently described to warrant repetition. The only point which bears emphasis, however, is based upon the work of Meinkoff<sup>2</sup> who showed the variations and the relation of the costophrenic angle to the

twelfth rib. Based on this work the skin incision is made along the course of the twelfth rib, but the incision through the rib bed should change its course to a transverse one. The latter is made at the level of the spinous process of the first lumbar vertebra, thus avoiding contamination of the pleural cavity.

#### CONCLUSIONS

1. Six subphrenic spaces are described
2. This simplifies the surgical anatomy, diagnosis, and treatment of subphrenic infections
3. Diagnostic and therapeutic suggestions are presented

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days, except that the tensile strength of cotton remained practically unchanged from the original. There was a loss of chromic catgut of 30 per cent in four days, 50 per cent in seven days, and 60 per cent in ten days. A cotton suture No. 50 remaining in human tissue for eighteen days showed only a 10 per cent loss in strength.

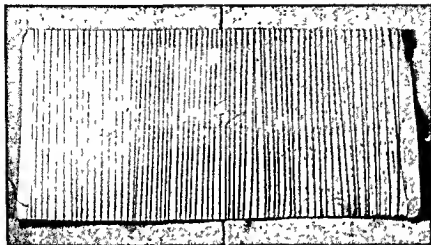


Fig 1—Cotton wrapped on cardboard preparatory to its being wrapped in sheet for sterilization. Size of cotton is marked on the cardboard and can be seen as No. 50.

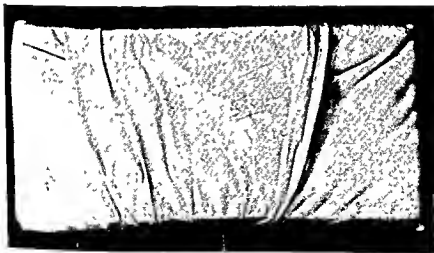


Fig 2—The card wrapped in cloth ready for sterilization in the autoclave at twenty pounds pressure for twenty minutes. This outer cloth is also marked as to the size of the cotton.

Absorbable sutures produce essentially a wet reaction in tissue which is an attempt on the part of the host to digest the sutures by means of proteolytic ferments derived from leucocytes. This wet reaction consists of excessive fluid and cellular exudate which is associated with a delay in the appearance of

fibroblasts. Both of these factors slow wound healing. Nonabsorbable sutures produce a minimum of exudate (dry reaction) with early fibroblastic proliferation. When wounds are closed with cotton the tissue reaction is minimal and fibroblasts appear earlier. Fibroblastic proliferation occurs in five to seven days with catgut and in two days with cotton.

The material we used in this series, and which we are still using, was regular white sewing cotton, sizes 8, 30, and 50.

A cardboard is selected, seven by twelve inches. Along the twelve inch sides nicks are cut about one-eighth inch apart. The cotton is wound on the cardboard in these nicks. The card wrapped with cotton is then covered with a cloth and labeled as to size. The cardboard is used in sterilization since it bends as the heat contracts the cotton and the threads will not break. The sterilization is done in the autoclave at twenty pounds' pressure for twenty minutes. On removing the card containing the cotton from the sterile cloth the cotton strands are cut in the long axis of the cardboard by the sterile nurse. This produces fourteen-inch lengths of the suture material (Figs. 1 and 2).

The cases selected for this study were taken from the first group of hernias repaired with cotton sutures so that we would have at least a four-year follow-up. The catgut series was selected for about the same period of follow-up. For both catgut and cotton groups we chose primary inguinal hernias; no recurrent hernias were selected in either series.

The age groups were fairly similar and are expressed in Table I.

TABLE I. AGE GROUPS

YEARS	COTTON	CATGUT
12 to 20	12	8
20 to 30	24	26
30 to 40	27	23
40 to 50	22	15
50 to 60	16	18
60 to 70	3	5
70 and upward	0	1

The operations were performed by members of Surgical Service B and the same technique for repair was used in all the cases (Bassini). For suturing the conjoined tendon to the shelving margin of Poupart's ligament, No. 8 cotton was used. The aponeurosis of the external oblique was sutured with No. 30, and No. 50 was used for ligatures.

The incidents of male and female, and right and left inguinal, in the 200 cases are shown in Table II.

No strangulated hernias were included in either group.

The postoperative temperature reactions of cotton and catgut in herniorrhaphy have been described by Zollinger and Flynn.<sup>1</sup> They found that the

TABLE II.

	MALE	FEMALE	RIGHT	LEFT
Cotton (100)	91	9	79	30
Catgut (100)	94	6	60	40

first postoperative day temperature was 99.4° F with cotton as compared with 100.0° F with catgut. They further found that a normal average temperature was attained, in cases in which cotton was used, on the fourth postoperative day as compared to the sixth postoperative day for those with catgut.

Our experience shows that the first postoperative day temperature was 99.6° F. with cotton and 99.5° F with catgut. In both types of cases normal average temperatures were attained on the fourth postoperative day. Thus, we find very little difference in the two groups so far as temperature reaction is concerned.

Far more important than temperature reaction, we believe, is the immediate postoperative condition of the wound and the permanent result of the herniorrhaphy. First, in regard to the appearance of the wound, Shambaugh<sup>8</sup> showed incidents of suppurative wounds to be twice as great following the use of catgut as following silk. The wounds in which cotton was used in our cases showed some reaction (redness) which disappeared on the second postoperative day. Those in which catgut was used showed a reaction not only of redness but of edema and induration persisting until the tenth to fourteenth postoperative day. Our feeling is definitely that cotton gave a much less local reaction than did catgut regardless of the equality of the patients' temperature reactions.

Our study of complications between the cotton and the catgut series confirms this statement. As to wound complications with cotton, we had one case (1 per cent). This patient had a hematoma of the wound, which we believe, was due to faulty technique in not having a dry wound at closure. In the catgut series, however, we had ten cases (10 per cent) with wound complications. Four were infected wounds and six involved serum collections in the wounds. This contrast was the most striking of all in our study and we believe this alone justifies the use of cotton sutures.

Other complications were limited to the respiratory tract, testicle, and urinary bladder. A comparison of cotton and catgut complications is shown in Table III.

TABLE III. COMPLICATIONS IN CATGUT AND COTTON SERIES

CATGUT			COTTON		
NUMBER	COMPLICATION	ANESTHESIA	NUMBER	COMPLICATION	ANESTHESIA
6	Serum collection	Spinal	1	Hematoma	Cyclopropane
4	Wound infections	Spinal	1	Atelectasis	N <sub>2</sub> O Ether
1	Orchitis	Spinal	3	Upper respiratory	Spinal
1	Pleurisy	Spinal	1	Orchitis	Spinal
2	Cystitis	Spinal			

The predominant anesthesia for both groups was spinal, representing 70 per cent of both groups. The other 30 per cent consisted of local and general anesthesia.

As to the permanency of results of the total 200 cases, follow-up studies were done on all of them. These follow ups represent three- to four-year postoperative checks. In the catgut series there were six recurrences (6 per cent). There were four recurrences in the cotton series (4 per cent). This represents a reduction of recurrences of one third which is, we believe, significant. Meade

and Long,<sup>9</sup> in a study of 465 consecutive wounds in which cotton suture material was employed, demonstrated cotton to be highly satisfactory in its clinical application. We believe that our work with cotton bears out their findings. For the past six months we have been using cotton suture material in all abdominal operations associated with early ambulation and expect to report on this experience in the near future.

In summary, a review of the literature has been reported regarding cotton as a suture material.

We have presented a contrast study of 100 consecutive uncomplicated inguinal hernias repaired with cotton and 100 consecutive uncomplicated inguinal hernias repaired with catgut.

The same type operation was done in all cases in both groups (Bassini).

All of the operations were done by members of Surgical Service B staff.

In conclusion, our findings substantiated the findings of other workers favoring cotton as a suture material.

There was less tissue reaction in the wounds sutured with cotton.

There was no difference in temperature reaction in the two groups.

There were fewer wound complications with cotton sutures.

The recurrence rate was reduced one-third in the cotton series.

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## DISLOCATION AT THE ACROMIOCLAVICULAR ARTICULATION

### A NOTE ON TECHNIQUE OF RADIOGRAPHIC EXAMINATION OF THE SHOULDER IN SUSPECTED DISLOCATION AT THE ACROMIOCLAVICULAR OR HUMEROSCAPULAR ARTICULATION

LIEUTENANT COLONEL CHARLES J. SITRO, MEDICAL CORPS,  
ARMY OF THE UNITED STATES

ON NUMEROUS occasions we have noted on physical examination the existence of a dislocation at the acromioclavicular articulation and the absence of such findings on simultaneous radiographic examination of the part. This was noted especially when the radiographic examination was made with the patient in the recumbent position. On further investigation we observed that in a fresh dislocation at this joint, there is a tendency for the clavicle to realign itself into a normal relationship with the acromion when the patient is in a recumbent supine attitude.<sup>1,2</sup> Similarly, radiographic examination of the shoulder taken in the recumbent position has failed to demonstrate a coexisting partial subluxation of the humeral head\* (Fig 1). For this reason we have added the following technique for the radiographic examination of the shoulder area. The patient stands or sits for two or three minutes with the unsupported affected upper extremity held at the side of the body or chair. A five- to ten-pound weight is then placed in the hand of the affected extremity in order to permit gravity traction to the shoulder area. During a three-minute period of such traction, radiographic examinations are made of the shoulder in the anteroposterior projection with the arm in external and internal rotation and the chest in a neutral as well as in a 15 degree oblique attitude (Fig 2). These views permit visualization of the humeroscapular joint space and of the subchondral regions of the acromioclavicular articulation†.

A brace was used in the treatment of recent subluxations at the acromioclavicular articulation (Fig 3). The double straps which extended over the acromioclavicular articulation permitted easy correction of the upward elevation of the acromial end of the clavicle (Fig 4). The position of the platform for the upper extremity could be readily modified so as to alter the angle of abduction both in the sagittal and coronal planes<sup>3,4</sup>. This brace was worn from six to eight weeks and was applied in the treatment of fourteen patients with excellent results. No surgical intervention was necessary.

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\*A patient who was treated at another hospital for a dislocation at the acromioclavicular articulation by surgical intervention complained of pain in the same shoulder. The clinical examination of this area revealed a well healed scar and a fair range of active and passive motion at the affected shoulder. Radiographic examination disclosed good alignment of the acromion to the clavicle, the presence of wire sutures, and slight irregularity in the subchondral region of these two bones. After two minutes of suspension traction of five pounds to the affected upper extremity, an incomplete subluxation of the ipsilateral humeral head was noted on radiographic examination (Fig 1).

†In the oblique view one was able to detect a small area of destruction in the acromion as the result of an infection. The other views failed to demonstrate its presence.





FIG 1—Radiograph (retouched) of the shoulder taken with the patient in a standing attitude with ten pounds of gravity traction to the affected upper extremity. *A*, Note the dislocation at the acromioclavicular joint. In radiographic studies made in the recumbent position, no dislocation was observed in this articulation. *B*, In another patient who was treated for a dislocation at the acromioclavicular articulation, gravity traction to the upper extremity revealed a downward partial luxation of the humeral head (see footnote page 751).



FIG. 2—*A* and *B*, Photographs show the method of applying traction to the upper extremity in the standing and sitting attitudes.

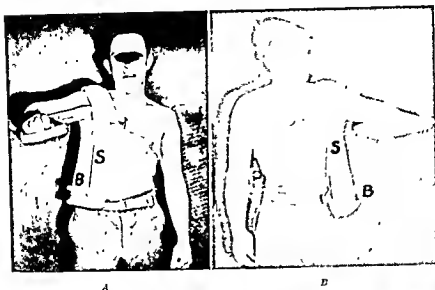


Fig 3 A and B—Photographs show brace from front and back views

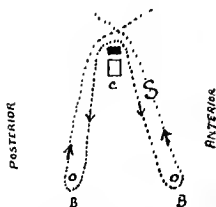


Fig. 3C.



Fig. 4.

Fig 3 C—Diagram shows the direction of the forces that the double web strap (*S*) exerts on the clavicle (*C*). The black rectangle over (*O*) is a piece of heavy felt. (*B*) is the metal rod on the brace. See Fig 3 A and B.

Fig 4—Radiograph (retouched) reveals normal alignment of the clavicle to the acromium. The dislocation as noted in Fig. 3, A was corrected by the brace.

## CONCLUSION

It is suggested that the radiographic examination of the shoulder be made with the patient in a standing or sitting attitude. The affected unsupported arm should be given gravity traction by holding a five- to ten-pound weight in the hand for two or three minutes. By this technique one can readily detect incomplete and complete separations at the acromioclavicular joint. In certain instances, this method has revealed a partial downward subluxation of the humeral head when other examinations have failed to demonstrate any abnormality.

For treatment of dislocation at the acromioclavicular articulation, we have used a brace which readily corrects the elevation of the acromial end of the clavicle.

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## TRACHEOTOMY IN MAXILLOFACIAL SURGERY

MAJOR GEORGE A. FRIDMAN, MEDICAL CORPS, ARMY OF THE UNITED STATES

SEVERE maxillofacial wounds are often associated with other injuries. Associated neck injury is especially important in this connection. These extensive injuries tax the combined judgment of the plastic and the oral surgeon, and the anesthetist. Three questions must be answered immediately: (1) How much can we do? (2) How much shall we do? (3) How best shall this be done?

Complete and proper preoperative diagnosis, including over-all evaluation of the injury, answers the first question. The patient's general condition may preclude anything but the most minor repair, even where there is extensive maxillofacial injury. There may be serious intracranial, abdominal, or thoracic complication, which may take precedence in operative importance and priority. Because of a military situation, the patient may arrive in the operating room hours after the original injury was sustained. The facial tissues may be full of debris, clothing, or dirt. The removal of certain fragments, such as those impinging upon the facial nerve, may inflict more harm than their presence.

A mental picture and understanding of the follow-up treatment necessary answer the second question. It may be feasible, in certain cases, not to attempt removal of a foreign body, even when it is lodged in the pharynx. Shall the wound be closed by primary suture? Shall a graft be attempted as primary treatment in a forward hospital with all things considered? Shall tracheotomy be done? Each case may be judged on its own merit.

The indicated anesthesia answers the third question. General anesthesia may be necessary in wounds involving the buccal cavity, pharynx, larynx, and in many cases extensive soft tissue wounds. Pentothal anesthesia is contraindicated in these cases where the aspiration of blood, teeth, mucus, or debris must be prevented. Endotracheal anesthesia is the method of choice, because it provides a free airway, a packed-off larynx, and freedom in the field of operation. Smooth anesthesia enables the surgeon relaxedly to accomplish more in less time, without hurry. The anesthetist must be skilled in the technique of intubation. Trendelenburg<sup>7</sup> first used this method of anesthesia in 1869, already having ascertained the value of a packed-off pharynx in operations around the oral cavity. Before operation tracheotomy was performed and the administration of the anesthetic continued by means of a cannula surrounded by an inflatable cuff inserted into the trachea through the wound. McEwen,<sup>8</sup> a surgeon in Glasgow, introduced the present type of endotracheal anesthesia for operations on tumors at the base of the tongue. Chevalier Jackson, in 1913, described laryngoscopy and the impetus given to this form of anesthesia during the last war made endotracheal anesthesia the method of choice, wherever bleeding into the air passage was a possibility.

The first-aid and preoperative management of these cases is designed generally and primarily toward saving the life of the patient. An airway must be maintained and hemorrhage controlled. Shock treatment is instituted and the patient made as comfortable as possible by splinting and bandaging. The administration of tetanus toxoid or other necessary medication is carried out. The neurosurgeon routinely examines these patients to eliminate the possibility of the presence of intracranial involvement. Other injuries, whether orthopedic, thoracic, or abdominal, are diagnosed for relative importance in relationship to the maxillofacial situation. This cooperative diagnostic effort has made possible a mortality of two maxillofacial cases at this hospital out of a series of several hundred. If possible, and the patient can be turned, roentgenologic study includes views in the lateral, posteroanterior, and occiputomenal planes. Three views have proved of definite value in the diagnosis of these cases. The oral surgeon examines the patient and ascertains the amount of dental involvement and, in concert, a combined plan of operation is decided upon. After premedication, the patient is taken to the operating room.

Indications for tracheotomy are as follows: (1) Acute respiratory obstruction is already present, which cannot be relieved by other means. (2) Respiratory obstruction is not yet present, but may occur either during or after operation.

The causes for acute respiratory obstruction are:

- 1 Falling back of the tongue, which may occur in unconsciousness or in certain mandibular fractures. The tongue acts as a check valve according to Chevalier Jackson, at the laryngeal opening. It is forced by each respiration after which it immediately falls back into its gravity position. Attempts at inspiration draw it over the laryngeal entrance and obstruct the ingress of air. Relief may be obtained by holding the jaw forward and so carrying the tongue away from the laryngeal opening.

- 2 Foreign bodies over the laryngeal aperture. Their removal is necessary under direct vision because in these cases where they become impacted in the pharynx, death may ensue before they are removed. In some cases, tracheotomy is necessary.

- 3 Edema of the aryepiglottic folds due to the spread of infection from neighboring structures. This condition may exist preoperatively but may also be a postoperative complication as the result of the spread of inflammation.

- 4 Adduction of the vocal cords caused by anoxial spasm of the laryngeal muscles. The muscles which adduct and abduct the cords, like all other muscles, work smoothly only when their oxygen supply is adequate. It is likely to occur in unpremedicated anesthetic-resistant individuals. At low levels of oxygen tension, anoxemic spasm of some muscle groups may occur. Spasm may also occur from attempts to intubate the uncannalized larynx under light pentothal anesthesia. The respiratory center is already depressed and the spasm may cause acute respiratory obstruction. This condition may be relieved by the administration of oxygen.

- 5 Hemorrhage into the air passage, which may cause acute obstruction unless controlled.

6. Direct or indirect injury to any segment of the upper respiratory tract. The signs of acute respiratory obstruction are

1. Extreme dyspnea, because respiratory movements have ceased to be effective even though they may continue for a few seconds
2. The use of the accessory muscles of respiration with an indrawing of the suprasternal and supraclavicular notches.
3. Cyanosis and extreme congestion of the face because the veins at the root of the neck are constricted.
4. Increase of venous engorgement, although the heart continues to beat for some minutes after respiration has ceased, because blood is forced into the vessels, but its return to the heart is not aided by the pumplike mechanism of the thorax.

In war surgery, we are primarily concerned with indications for tracheotomy, where respiratory obstruction is not yet present but the diagnosis leads us to believe that it shall ensue. Respiratory obstruction may arise in some of the following categories

1. Injuries to the base of the tongue, pharynx, or larynx, with or without the presence of foreign bodies.
2. Large foreign bodies in the air passages where they cannot be removed under direct vision.
3. Extensive soft tissue wounds of the face which may cause later destruction by the spread of inflammation to the mucous membranes of the air passages.
4. Extensive fractures of the mandible where the tongue cannot be held forward by mechanical means.
5. Extensive injury to the upper facial regions, especially when these close off completely the nasal passage, or in severe fractures of several of the upper facial elements. Postoperative inflammation may descend to involve the pharynx and subsequently the mucous membranes of the air passages.
6. Injury to the recurrent laryngeal or the vagus nerves by direct trauma or by pressure from hemorrhage may cause paralysis of both cords if bilateral and extreme dyspnea may ensue.
7. Surgical emphysema and parapharyngeal infection may occur as sequelae of penetrating wounds of the neck according to Bailey.<sup>1</sup> The former is likely to occur when there is unrelieved laryngeal obstruction, and forced inspiration sucks air into the fascial layers with distention of the tissues. If air enters the mediastinum, respiratory embarrassment ensues which must be relieved by tracheotomy. Parapharyngeal infection, when it occurs, must be opened by a vertical incision over the sternal insertion of the sternocleidomastoid. Tracheotomy may also be necessary.

Gray's<sup>4</sup> *Description of the Anatomy of the Trachea*.—The trachea extends from the cricoid cartilage at the level of the sixth cervical vertebra to its bifurcation into two bronchi, at the level between the sixth and eighth thoracic vertebrae. In the adult, it is a cartilaginous and membranous tube not quite cylindrical, four to five inches long, and approximately one-half its length is



The trachea is more deeply placed as it descends and also below this point larger blood vessels may be encountered. Orderly and planned tracheotomy, where time is at hand, is carried out under local anesthesia.

The position of the patient is extremely important. A pillow or sandbag is placed under the shoulders and the head is thus extended. The trachea is thus brought forward closer to the operative field and is fixed.

The operative field is made sterile. The midline of the neck is palpated, the position of the thyroid and the cricoid cartilages rapidly ascertained, and the position of the thyroid isthmus found. The skin is infiltrated with 2 per cent procaine with eight minims of epinephrine to the ounce. The subcutaneous structures are also infiltrated.

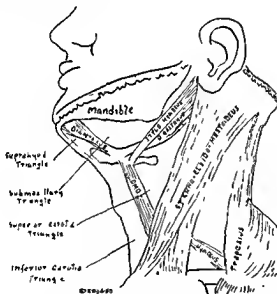


Fig 3.—Triangles of neck showing the inferior carotid triangle in which tracheotomy is performed

A horizontal<sup>3</sup> incision is made, one inch long, equidistant from the midline just below the level of the thyroid isthmus. The horizontal incision is the natural incision in all operations on the neck. Experience has shown that these operations heal more satisfactorily than where the vertical incision has been made. In emergency tracheotomy where time is at premium, a vertical incision may be permissible. After the skin incision, exactly in the midline, a vertical incision is made into the fascia. If necessary, more anesthetic can be infiltrated into subcutaneous tissues. In healing, the subcutaneous reapproximation in one plane, and the skin in another, produces a wound exactly the size of the tracheotomy tube. Bleeding is a prominent feature of the operation and is due largely to the engorgement of the tissues because of the resistance to the venous return to the thorax. All bleeding vessels are retracted laterally, and if the thyroid isthmus happens to be in the field of



operation, it is retracted upward, but if the original incision was made properly, this will not be necessary. The pretracheal fascia is incised, and the trachea is recognized as a glistening, pink, longitudinal structure. With the trachea under direct vision, a vertical incision is made upward into the anterior surface. The trachea must not be separated from its surrounding structures since this shall interfere with its blood supply.<sup>2</sup> A suction apparatus may be needed when the trachea is opened and is to be held in readiness. A small amount of procaine may be injected into the tracheal wall and lumen. Cocaine has been suggested, but we have had no experience with it. A perfectly dry field is desirable and blood should not get into the trachea. The incision into the trachea is made in an upward direction to avoid cutting too deeply into the trachea and possibly injuring the esophagus. If conditions are favorable, a small oval window is made in the trachea, since this precludes pressure on the tracheal wall and there may be sloughing of cartilage pressed against the tube. The tube is guided with care into the aperture which is spread by a tracheal retractor by means of an introducer. It is easy to place the tube either to the front or to the side of the trachea. After the tube is in position the introducer is withdrawn and the inner tube is inserted. The stimulus of opening the trachea may cause a bout of coughing, which may expel mucus or start bleeding. The suction apparatus draws off any accumulation of mucus. If there is prolonged bleeding it is necessary to ligate the vessel. The field should be absolutely dry before the patient leaves the operating room. If at any time respiration ceases, artificial respiration is started. If the original incision has been made properly, no suturing of the skin should be necessary; however, one or two sutures may approximate the lateral boundaries of the original incision. Petrolatum gauze is placed between the tube and the skin with the former fixed into position by tapes tied around the patient's neck. A layer of moistened gauze is placed over the front of the opening to prevent the inhalation of dust or foreign bodies. As an additional precaution, an additional tube and inner tube are tied around the patient's neck in the event that the first become clogged or dislodged by an explosive cough.

There are immediate dangers to the operation, which must be avoided. The operator must adhere to the midline of the neck, or the great vessels may be incised. Incision into the esophagus causes a fistula with subsequent mediastinitis and possibly fatality. There is the removed risk of stenosis, following operation, if the incision is made too high.<sup>3</sup> Chevalier Jackson reported that five sixths of his cases of chronic laryngeal stenosis, in the past thirty years, have been due to faulty tracheotomy or improper aftercare of the tracheotomy tube and wound. After emergency tracheotomy, sometimes performed without anesthesia, which involves the first ring of the trachea or the cricoid cartilage, it may be feasible to perform a secondary tracheotomy lower down to diminish the risk of stenosis.

*Aftercare*—The tracheotomized patient should never be separated from a suction machine until he reacts, if general anesthesia has followed. This patient should never be left alone until he becomes cooperative and is able to

take care of himself. He is instructed in the use, care, and function of the tube. This must not be allowed to become clogged by secretions, and it is suctioned out at regular intervals. The outer tube is changed daily to prevent ulceration and secondary hemorrhage. The gauze over the opening is kept in place. The ribbon should never be cut unless a medical officer or trained personnel are present. Sedatives and narcotics are used as sparingly as possible postoperatively, since the cough reflex is an important protective mechanism in preventing the accumulation of bronchial secretion.

#### CASE REPORTS

CASE 1.—J. R. was admitted to a field hospital in France, July 13, 1944. He had suffered an extensive gutter type, perforating through and through wound of the soft tissues of the right cheek. The shell fragment had caused some loss of tissue, but there was no bone involvement. Respiration seemed normal and the airway patent. Since there was no evidence of any respiratory obstruction, a tracheotomy was not performed.

Under pentothal anesthesia for induction, the anesthetist attempted to intubate the patient for endotracheal anesthesia. There was difficulty in getting the tube into the larynx and the patient developed respiratory difficulty during the procedure. The intubation which was attempted under barbitalurate anesthesia caused a laryngeal spasm. The respiratory center was already depressed and the administration of the anesthetic caused anoxic spasm of the adductor muscles of the larynx.

In this case preliminary tracheotomy might have saved the patient's life because inflammation which descended from above caused swelling of the aryepiglottic folds. The intubation caused the larynx to go into a spasm which could not be relieved. A tracheotomy would have prevented this additional trauma to the respiratory tract.

CASE 2.—A. P. was admitted to a field hospital in France, July 15, 1944. He had suffered a severe gunshot wound of the mandible. The wound of entrance was at the left angle of the mandible and the missile coursed along the base of the tongue, lacerating it as well as the left posterior tonsillar pillar. The bullet had traversed the buccal cavity from the left to the right and lodged itself in the tissues of the right cheek. Examination revealed an extensive laceration of the tongue and edema of the aryepiglottic folds. X-ray examination showed a complete, compound, comminuted fracture of the right ramus of the mandible.

*Operation*—Horizontal tracheotomy was performed under local anesthesia. Nitrous oxide oxygen ether was administered endotracheally through the tracheotomy tube as in Fig 4 and the larynx packed. The lacerations of the tongue and left tonsillar pillar were sutured and the bullet was removed from the right cheek introrally. The right buccal mucous membrane was approximated. The wound of entrance was debrided minimally and closed by primary suture. A rubber drain was inserted under the inferior border of the right angle of the mandible up to the fractured area. The fractured mandible was fixed by means of intermaxillary continuous loop wiring with intramaxillary elastics.

The patient had an uneventful postoperative course and was evacuated to the zone of the interior. The tracheotomy was the key to the ease with which the situation was handled.

CASE 3.—S. F. was admitted to a field hospital in France, July 16, 1944. The patient had received multiple, severe shell wounds which had penetrated the face and neck. He was suffering from marked dyspnea upon admission with obvious respiratory obstruction. This was caused by a concomitant esophageal injury and the tentative diagnosis was tracheoesophageal fistula. The indication for tracheotomy was self evident because of the marked dyspnea in connection with a trauma to the neck.

*Operation.*—Horizontal tracheotomy was performed under local anesthesia. There was a continuous escape of brownish intestinal contents through the tracheotomy tube which confirmed the diagnosis of tracheoesophageal fistula. Gastrostomy to divert the intestinal contents as a preliminary was decided upon before attempted repair of the fistula. The patient's condition became steadily worse and he died even before this was done.

Two other patients with tracheoesophageal fistula came under our observation. In both of these cases the patients died before operative interference.



Fig. 4 (Case 3).—An example of extensive facial injury. Anesthesia is being given endotracheally by means of a tube extending into the tracheotomy tube. Anesthesia was given this way in Case 4 also.

*CASE 4.*—H. W. was admitted to a field hospital in France, July 22, 1944. He had suffered multiple shell wounds of the perforating type which caused the following: fracture compound, comminuted of the right and left frontal sinuses, orbits, malar zygomatic compounds, maxillary antra, nasal bones, and maxillary frontal processes. There was maceration of the right and left eyes.

Tracheotomy was indicated although the upper facial elements were involved because the severity of the injury would have made the maintenance of a normal airway impossible postoperatively. The operation itself could not have been performed without it. Thus, a tracheotomy was performed under local anesthesia and the anesthetic administered through the tube (as in Case 2 and illustrated in Fig. 4). The frontal sinuses were irrigated, mucous membranes exenterated, and drainage established to the outside. By means of the Caldwell Luc approach on both sides, the mucous membranes of both maxillary antra were exenterated. The maxillary elements were elevated and repositioned and both antra packed with petrolatum gauze. Drainage was thus established from above into each

superior gingivolabial sulcus. The maxilla was wired by means of continuous loop wiring and splinted upward by bandaging and pulling up of the mouthpiece.

The postoperative course was uneventful and the patient was evacuated to the zone of the interior.

CASE 5.—H. H. was admitted to an evacuation hospital in France, Aug 15, 1944. He had suffered a severe gunshot wound which had perforated the neck. There was a massive hematoma on the left side of the neck. He had marked dyspnea due to the pressure on the recurrent nerves or the aorta.

The indication for tracheotomy was present and it was performed under local anesthesia. The hematoma was drained to the outside.

The patient was given supportive therapy. His condition improved and he was evacuated.

CASE 6.—J. C. was admitted to an evacuation hospital in France, Aug 25, 1944. There was a severe perforating gunshot wound of the neck with laceration of the common carotid artery. The patient's condition was critical upon admission.

Horizontal tracheotomy was performed under local anesthesia which relieved the patient's dyspnea. The common carotid was ligated under general anesthesia. The patient died twelve hours after operation.



Fig 5 (Case 7).—Preoperative view of patient showing extensive soft tissue involvement of right cheek and upper lip.

CASE 7.—C. M. was admitted to an evacuation hospital in Holland, Oct. 4, 1944. He had suffered extensive facial injury as shown in Fig 5. The following diagnosis was made: There were compound, comminuted, complete fractures bilateral of the mandible and of the right maxilla. The wound of the right cheek was extensive, of the gutter type, and

extended into the upper lip where there was a loss of tissue. The tongue was severely lacerated. There were, in addition, a lacerated wound of the scalp and a penetrating wound of the left groin.

Tracheotomy was indicated because respiratory obstruction would have developed although not present. It was performed under local anesthetics and the anesthesia administered through the tube. The lacerations of the tongue were sutured. The maxilla was wired by the dental surgeon by means of continuous loop wires. Arch bars were wired



Fig. 6 (Case 7) —Postoperative appearance of patient on operating table, note tracheotomy tube.

to the teeth of the mandible. Fixation of the mandible to the maxilla by means of intra maxillary elastic traction was effected after the patient recovered from the anesthetic. The dental work was performed in this sequence so that there would be no interference with the suturing of the soft tissues of the face. The facial wound was débrided as conservatively as possible and the wound closed by primary suture. The upper lip was grafted by means of full thickness skin taken from behind the ear (Fig. 6). The scalp and groin wounds were cared for. A transfusion of 1,000 c.c. of stored blood was given the patient during operation.

The postoperative course was uneventful. He received an additional 500 c.c. of blood and the same amount of plasma. The graft and wound were in good condition when the patient was evacuated after five days of hospitalization in good condition.

CASE 8—R. W. was admitted to an evacuation hospital in Holland, Oct. 7, 1944. He had suffered a severe perforating wound of the face with complete loss of outer nose as well as the bony and cartilaginous nasal elements (Fig. 7). There was skin loss of the upper lip as well as of the symphysis of the mandible. The maxilla was fractured on both sides. The patient seemed to have a patent airway and it did not seem necessary to perform tracheotomy.

Intubation was through the mouth and endotracheal anesthetic was administered. The wound area was debrided and bilateral intranasal antrostomy performed for the drainage of both maxillary antra. The outside skin was approximated to underlying mucous membrane circumferentially. Fixation was accomplished (as in Case 7).



Fig. 7 (Case 8)—Loss of nasal elements and loss of skin over symphysis of mandible. tracheotomy was necessary in this case postoperatively

Forty-eight hours after operation the patient was observed to be experiencing difficulty in breathing. There was probably a combination of inflammation as well as mechanical interference, because of the packing of the nasal area and the fixation.

Horizontal tracheotomy was performed the same day under local anesthesia. The patient did well and was later evacuated in good condition. This is another example for the necessity of tracheotomy when the upper facial elements are involved.

CASE 9—R. J. was admitted to an evacuation hospital in Holland, Oct. 22, 1944. He had multiple penetrating shell wounds. There were severe wounds on the right cheek and ear. There was a penetrating wound of the neck posteriorly at the level of the fourth cervical vertebra (Figs. 8 to 10). There were severe fractures of the right maxilla and malar zygomatic compound and also an incomplete fracture of the right condyle of the mandible. Multiple metallic foreign bodies were imbedded in the right cheek and right mastoid region. In addition, there was hemorrhage as well as a blast injury of the left leg.

Because of the patient's general condition and the lung injury, local anesthesia was decided upon. The foreign bodies were removed from the neck and mastoid region and a rubber drain was inserted in this area. The right cheek and ear were sutured. The neck

wound was débrided. Eyelet wires were applied to the teeth, and intramaxillary elastic traction was applied for stabilization of the mandibular fracture.

The following day the patient suffered from dyspnea. There was swelling of the aryepiglottic folds. Under local anesthesia, a tracheotomy was performed at which time 500 cc of stored blood were administered. He was evacuated on November 4 in good condition.

Fig. 8



Fig. 9

Fig. 8 (Case 9)—Lateral x-ray view showing fractures of maxilla and mandible. Several metallic foreign bodies are scattered throughout, note the foreign body posteriorly at the level of the fourth cervical vertebra.

Fig. 9 (Case 9)—Lateral x-ray view. Note the foreign body in the oropharynx, necessitating postoperative tracheotomy, though it was not removed.

CASE 10—M. A. was admitted to an evacuation hospital in Holland, Oct. 18, 1944. There was a shell wound which had perforated the neck. The point of entrance was below the left angle of the mandible and the missile had coursed along the floor of the mouth.

The exit was below the right angle of the mandible. There was a perforating wound of the pharynx at the level of the epiglottis.

Under endotracheal anesthesia, the pharyngeal perforations were closed by means of exploration from the outside from one mandibular angle to the other across the hyoid bone. Ligature of the right lingual artery was necessary because it bled profusely into the pharynx after it had been severed by the missile.

Tracheotomy was necessary postoperatively because the patient developed dyspnea. It would have been better performed preoperatively. The patient was later evacuated in good condition.



Fig. 10 (Case 9).—Occipitomental view clearly showing fracture of right malar-zygomatic compound. The trachea is seen clearly.

**CASE 11.**—A patient was admitted to an evacuation hospital in Holland, Jan. 12, 1945. An aerial bomb had caused a perforating wound of the neck (Fig. 11). The wound of entrance was posterior and the wound of exit anterior where there was a large, gaping, lacerated wound in the posterior triangle of the neck.

The wound was debrided, and primary suture of the wound of exit was effected (Fig. 12). A rubber drain was inserted into the wound of entrance. The patient had an uneventful postoperative course and was finally evacuated.

This case is cited as an example of severe neck wound in which tracheotomy was not indicated. The wound was lateral to the great vessels of the neck and did not involve them. The airway was not impinged upon and there was no respiratory obstruction.

Note that in these cases only the salient points were included. Local sulfadiazide or penicillin were used in most cases. Postoperatively, the patients received penicillin and sulfadiazine.



FIG. 11.



FIG. 12

Fig. 11 (Case 11) —Perforating wound of neck showing large lacerated wound of exit and wound of entrance posteriorly, injury involves the posterior triangle of neck (see Fig. 3)

Fig. 12 (Case 11) —Postoperative view of patient on operating table. Endotracheal anesthesia is being given through a tube in the right nostril. The wound has been closed in layers by primary suture. Note the rubber drain in the wound of entrance.

## SUMMARY

1. Tracheotomy is not an operation without hazard and should not be performed unless indicated. When necessary it may be the most important factor in saving the life of the patient.

2. Acute respiratory obstruction when present, and which cannot be relieved by other means, is an obvious indication for tracheotomy. This may occur in (a) penetrating or perforating wounds of the neck because of involvement of the trachea, larynx, pharynx, or the base of the tongue, or (b) secondary involvement of these structures without direct violence, that is, inflammation.

3. Tracheotomy may be indicated in extensive soft tissue injury of the face because of postoperative respiratory obstruction caused by the spread of infection with resultant inflammation and edema of the airway.

4. Tracheotomy may be indicated in extensive involvement of the upper facial bony elements. Postoperative obstruction may be caused by mechanical means or there may be secondary involvement of the pharyngeal structures by the secondary spread of infection.

5. Tracheotomy is sometimes indicated in gunshot wounds of the mandible where there is extensive injury.

6. Proper aftercare as well as care in transit of tracheotomized patients is as important as the operation itself.

7. Case reports typifying these have been presented.

8. Horizontal incision of the skin is the natural and best one for tracheotomy.

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## PLEURALIZATION OF THE LEFT BRONCHUS IN PNEUMONECTOMY

ROGLIO BARATA, M.D., HAVANA, CUBA

*(From the University Hospital and the Children's Hospital for Tuberculosis)*

THE difficulties encountered in my first pneumonectomies regarding the inadequate pleuralization of the left bronchial stump, especially in cases of abscesses and bronchiectasis, led me to follow a technique, with such good results, that I believe it should be published.

*This procedure always permits the effective pleuralization of the left bronchus whichever the case for the surgical intervention might have been.*

It is known that in the left pulmonary pedicle, the anterior pleural flap leaves the mediastinum at the level of the posterior face of the ascending aorta and the posterior pleural flap at the level of the anterior face of descending aorta, there being, between these two segments of the vessel, a distance, variable with the width of the aortic arch, which is always of such a magnitude that when the lung is resected the pleural flaps retire and do not obliterate the mediastinal opening. The efforts to move near the pleural flaps by interrupted sutures produce large lacerations in its surface, leaving the bronchus pleuralized in an incomplete way and, therefore, exposed to the opening.

This difficulty is almost unsurmountable in some cases of abscesses where the pleural flaps of the pedicle are inelastic. Experience has taught us that it suffices to apply to the bronchial stump (closed by interrupted sutures of silk or chrome catgut, better results with metallic suture, Surgaloy No. 30) a pleural flap of the pedicle, which should cover it completely to avoid the bronchial fistula, and also that pediculated flaps separated from the posterior parietal pleura are not so effective as the flaps from the pedicle.

### TECHNIQUE

Once the pneumonectomy is completed, and after the bronchus is closed (Fig. 1), the mediastinal pleura is separated with the forefinger, following the interior surface of the anterior pleural flap of the pedicle (Fig. 2) to about one inch past the level of the phrenic nerve and the superior diaphragmatic vessels. The phrenic nerve can, at this moment, be crushed above the level where the stitches will be passed.

Following this, various interrupted sutures are made from the posterior face and borders of the bronchus to the ample mediastinal pleural flap which has been made movable. The sutures pass over the phrenic nerve, which, serving as a pulley, will make the pleura descend without lacerations, thus making it possible to apply to the bronchus the pleural flap which will cover it completely (Fig. 3).

When the tying of sutures is being finished, the bronchial stump is displaced to the front, resting against the ascending aorta. If, as occurs in a few cases, a posterior pleural flap can be made use of, everything possible is done to bring about the pleuralization of the total mediastinum, although this is not really necessary to obtain satisfactory results.



Fig 1



Fig 2



Fig 3

Fig 1—The lung has been resected. (a) heart and pericardium, (b) descending aorta, (c) pulmonary artery, (d and e) pulmonary veins, (f) phrenic nerve and superior diaphragmatic vessels, and (g) pneumogastric nerve.

Fig 2—Dissection of the anterior pleural flap (k).

Fig 3—The bronchial stump has been pleuralized by suturing the phrenic nerve and pleura to the posterior face and borders of the bronchus. Note the displacement of the bronchus.

This technique has been successfully used in more than twelve cases. On some occasions, after tying the sutures, the ascending aorta has been slightly compressed, but apparently with no bad effects. This difficulty has been obviated by dissecting a major pleural flap and stretching it, so that it easily reaches the bronchial stump.

#### REFERENCE

- Barata, R. Estudio anatómico topográfico del pedículo pulmonar izquierdo y su aplicación a la cirugía pulmonar, *Rev. tuberc.*, Habana 7, 430-434, 1943.

## Book Reviews

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**Penicillin—Its Clinical Application.** Under the General Editorship of Professor Sir Alexander Fleming, M.B., B.S., F.R.C.P., F.R.C.S., F.R.S., Professor of Bacteriology in the University of London, St. Mary's Hospital, London. Pp 350. Illustrated. Philadelphia, 1946, The Blakiston Company. \$7.

It is fortunate and fitting that the individual responsible for the discovery of penicillin should edit a definitive monograph on the present status of penicillin for the clinicians. Although other books have been published on this subject, Fleming's effort is the most authoritative and up to date. Recognizing that he was a laboratory worker and not a clinician, Fleming has delegated the presentation of the clinical phases of the subject to various British clinicians. The introductory chapter by Fleming on the "History and Development of Penicillin" is excellent. He gives merited credit to the pioneering efforts of Raistrick and his associates, who endeavored to produce penicillin long before the workers at Oxford. The introductory chapter is followed by informative discussions on the chemistry of penicillin, methods of manufacture, and pharmacology of penicillin. Methods of assaying penicillin are detailed by Fleming in another chapter. Hudson, who is surgeon at Middlesex Hospital, presents a chapter on the treatment of generalized infection. His statement that there is "no definite evidence that organisms can become penicillin resistant" will not go unchallenged. This does occur, but, fortunately, not too commonly. The management of chest infections is discussed by Geare of St. Mary's Hospital and chest surgery by Sellers of the London Chest Hospital, the latter is particularly well done. There has been considerable discussion concerning the merits of penicillin in gas gangrene, and the presentation of Porritt and Mitchell indicates a wide and critical experience. They emphasize the major role of surgery in prophylaxis. The advantages of penicillin in osteomyelitis are detailed by Aird of the University of Edinburgh, and this section should be consulted by anyone interested in a good review of the subject. The use of penicillin in sepsis neonatorum is the most comprehensive and well balanced that this reviewer has seen. This also applies to the section on penicillin in brain and meningeal infections written by Wright of St. Mary's Hospital.

Each of the specialties is well represented in this monograph, including dentistry and veterinary medicine. One wonders why such an excellent review of the subject should conclude with a chapter on "Penicillin and the General Practitioner." It is superfluous and not too informative. Clinicians, in general, in the United States will not agree with the enthusiastic recommendations their British colleagues have for the local use of penicillin. Perhaps penicillin was widely utilized in this manner because of the relative scarcity of the drug, but more extensive experience has shown that the topical application of penicillin is too frequently followed by serious reactions of a hypersensitive type.

Sir Alexander Fleming merits congratulations for making this monograph possible. The publishers are to be commended for the make up of the volume. This work is recommended without hesitation to specialists and to general practitioners.

# SURGERY

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## Original Communications

### THE SURGICAL TREATMENT OF HYPERTENSION

#### III. THE "NEUROGENIC" VERSUS RENAL HYPERTENSION FROM THE STANDPOINT OF OPERABILITY

GEZA DE TAKATS, M.D., AND EDSON FAIRBROTHER FOWLER, M.D., CHICAGO, ILL.  
(From the Department of Surgery, University of Illinois College of Medicine, and St Luke's Hospital)

#### INTRODUCTION

ALL classifications of hypertension contain a differentiation between a non-renal and a renal type of hypertension. It is generally assumed that the so-called neurogenic type of hypertension is the ideal case for splanchnic nerve section. In fact, an effort has been made to differentiate the neurogenic from the renal hypertension by the response of the patient's blood pressure to high spinal anesthesia.<sup>1</sup> In addition, Grimson proposed total sympathectomy in man, because in his experimental neurogenic hypertension produced by section of the buffer nerves, more limited procedures such as splanchnic nerve section and dorsolumbar sympathectomy were of little avail.<sup>2</sup>

Our experience, however, has not supported the view that the nonrenal hypertensives do better after operation than the lesions with definable renal lesions. In our series of fifty cases recently reported elsewhere,<sup>3</sup> an attempt has been made to define these groups so that a comparison of results can be made between them (Table I). Naturally the extent of vascular damage, as developed by our grading, has a potent influence within the groups.

#### THE "NEURO-ENDOCRINE" GROUP

Experimentally a number of methods are known to produce acute or chronic neurogenic hypertension; they have been concisely summarized in the monograph of White and Smithwick.<sup>4</sup> Page<sup>5</sup> gave a classic description of a "dienecephalie" syndrome in man, consisting of flushing of the face and neck, excessive perspiration, tachycardia, and hyperperistalsis, much like the cat exhibits when its midbrain is stimulated. However, such cases readily merge with the endocrine group, notably the ones seen at the menopause. For this reason, for lack of concise endocrine assays, we have pooled the whole group of patients in whom a primary renal hypertension could be excluded.

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TABLE I. CLASSIFICATION OF PATIENTS SUFFERING FROM "ESSENTIAL" HYPERTENSION (FIFTY PATIENTS OPERATED UPON)

NONRENAL	NUMBER OF CASES	RENAL	NUMBER OF CASES
"Neurogenic"	3	Unilateral renal disease	4
Endocrine	2	Renal trauma	2
Atheromatous	3	Toxemia of pregnancy	6
		Pyelonephritis	3
		Scarlet nephritis	5
		"Rheumatic kidney"	3
Total	8		23
Unclassified	19		

It would seem reasonable to predict the postoperative results by blocking the extent of sympathetic outflow which one intends to remove surgically. Both spinal anesthesia<sup>7</sup> and paravertebral sympathetic block<sup>8</sup> have been suggested for this purpose. In the surgery of the sympathetics controlling the extremities this has certainly been the practice of our group.<sup>7</sup> However, our experience with these methods in hypertensives has not been satisfying. Elderly persons with arteriosclerosis with high pulse pressures due to a rigid, nondistensible aorta are notorious for the hypotensive effects of spinal anesthesia (Fig. 1). Splanchnic block by the posterior route, the dangers of which one of us has previously described,<sup>8</sup> may produce marked fall in blood pressure due more to the toxic reaction to procaine or to a vasovagal reflex than to the effect of blocking the vasoconstrictor fibers. And finally there seems to be a type of nonrenal hypertension in which diffuse arteriolar resistance is maintained in spite of blocking the sympathetics of the area (Case 4). Vasopressin of the posterior lobe of the pituitary, which is under nervous control, may be one such mechanism.\*

Germane to this discussion are the experimental findings of Walter and P'yoan<sup>9</sup> who, while trying to produce diabetes insipidus observed a persistent hypertension in a dog whose third ventricle was punctured in the midline. This dog had a pressure of 242/130 and gradually developed tortuous arteries and nicking of the veins in the retina. A 23 per cent cardiac enlargement took place in four months. Nembutal depressed the pressure to 120/60, the cold pressor reaction was exaggerated. Insulin hypoglycemia was followed by a marked pressor response. In contrast to this a dog on which the Goldblatt clamp had been used showed a fixed hypertension with not much variation in pressure after pressor or depressor stimuli.

To satisfy our criteria of nonrenal hypertension, the following findings were postulated.

1. Normal renal structure in a hypertension of long standing. Such cases have been reported before. Striking is the case of Shapiro<sup>10</sup> who found no evidence of any renal impairment at the autopsy of a woman who suffered from a hypertension of more than twenty-five years' duration. In our material, normal biopsies were reported in six out of thirty-five cases, an incidence of 17 per cent. In the series of Castleman and Smithwick,<sup>11</sup> 7 out of 100 patients

\*Hydin, H., and Verney, E. B. (*Quart. J. Exper. Physiol.* 27: 313, 1932) showed that inhibition of water diuresis can be obtained after emotional stress or muscular exercise, when the kidneys and adrenals are denervated and both splanchnic nerves cut.

were graded as having normal kidneys, and 21 per cent as having grade 1 (mild) involvement (Case 1).

2. History of a previous thyroidectomy for a toxic goiter, which occurred in six of our fifty-two patients. When blood pressures were available at the time of thyroidectomy, they were reported as being high, in fact, some thyroidectomies were undertaken to reduce blood pressure. Such thyroid stimulation presumably on a pituitary basis is suggestive of a pituitary type of hypertension, which Griffith and his associates have especially promulgated.<sup>12</sup> We present three cases of this type (Cases 2, 3, and 4).

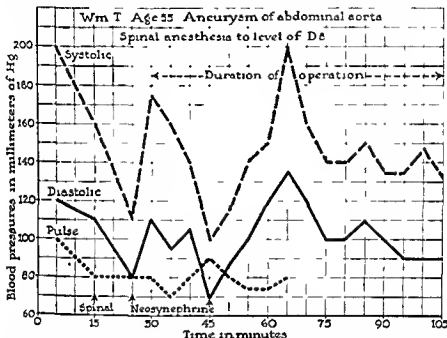


Fig. 1—Hypotensive effect of spinal anesthesia on a patient suffering from arteriosclerosis of the aorta. This patient's blood pressure fell from 200/120 to 110/80 mm. of mercury in twenty-five minutes. While the pressure was elevated with Neosynephrine temporarily, at the forty-fifth minute the pressure fell again to 100/70 mm. of mercury. Certainly this patient had anything but neurogenic hypertension, he had severe arteriosclerosis leading to a huge aneurysm of the abdominal aorta. The operation was not started until the first dip in pressure occurred, so that neither bleeding nor nervous stimuli from the field of operation could have been responsible for the hypotension.

3. Finding of a medullary or cortical tumor of the adrenal, which is not within the scope of this paper, can be best investigated by the combination of an intravenous pyelogram with air insufflation around the kidney (Fig 2) and the recently developed histamine response of such patients.<sup>13</sup>

#### CASE REPORTS

CASE 1.—M Z, 21 year old unmarried woman, entered St Luke's Hospital on June 15, 1941. With the exception of intermittent headaches, there were no complaints. One of these headaches was very severe, lasted a whole day, and was accompanied by nausea and vomiting. She had fallen from a horse several times, this was followed by dizziness for a day. There was some nycturia at times. She was rather high strung, temperamental, readily upset.



*Entrance.*—The patient's blood pressure was 160/100. Physical examination was negative. Eye grounds were normal. The heart occupied 40 per cent of the thorax. The electrocardiogram was normal. The urine was negative for pathologic elements. The intravenous pyelogram suggested a small and deformed left renal pelvis, but the retrograde pyelogram did not bear this out. Phenol-sulfonylthalein excretion was 35 per cent in one hour; the urea clearance was 58 per cent (standard). Blood chemistry was normal. Sodium amylal



Fig. 2.—Around the left kidney 200 cc of air have been injected in a 16-year-old girl with hypertension and hirsutism in whom a cortical adrenal tumor was suspected. This view was taken twenty-four hours later and shows a perfectly normal triangular shadow above the upper pole of the left kidney, separated from it by an envelope of air.

depressed the blood pressure from 170/104 to 135/90 mm. of mercury. The cold pressor test raised it from 160/100 to 190/120.

*Operations*—Operations were done on June 26 and July 9, 1941, at which time right and left splanchnic nerve sections were done together with a dorsolumbar sympathectomy. Both chains were cut between the ninth dorsal and second lumbar ganglia. The kidneys, ureters, and adrenals were normal. A biopsy, taken from the right kidney revealed no pathologic changes.

*Course*—The patient was discharged with blood pressures of 140/80, 120/80, and 80/0 in the three positions. The cold pressor response was minimal after the operation (140/80 to 145/80). She continued to have occasional headaches but lived a healthy outdoor life, taking on the job of a wrangler on one of the western ranches. The blood pressures fluctuated between 160/130 systolic and 100/80 diastolic during the next three years. Postural hypotension had disappeared. In May, 1944, she had a spell of unconsciousness with a blood pressure of 90/60 mm. of mercury, from which she temporarily recovered, but died suddenly in a second attack on May 23, 1944, not quite three years after operation. At autopsy no anatomic cause for death was found. The kidneys both grossly and microscopically were normal. Nothing was found in the brain.

*Comment*.—This was a case of a nonrenal hypertension, for which no cause could be found at autopsy. Note that a complete splanchnic section did not materially influence the blood pressure for the follow up period of three years. This observation will be later discussed on the basis of other "neurogenic" cases.

*CASE 2*—R K, a 24 year old white man, was admitted to the Research and Educational Hospitals on Jan. 25, 1941, complaining of nervousness and tremor.

*Past History*—He had been nervous and jittery ever since he could remember. Two and one-half years before, at the age of 22 years, he had an eye infection, at which time a systolic blood pressure of 140 mm. of mercury was discovered. He was referred then to the University Dispensary where a blood pressure of 170/110 and a basal metabolic rate of +27 per cent were discovered. No treatment was described and the blood pressure dropped to 132/76. One year before admission a blood pressure of 210/120 was obtained which fell on bed rest to 135/80. Other past history was not contributory.

*Entrance*—The patient's blood pressure was 150/90 mm. of mercury. The fundi were negative. The heart and electrocardiogram were normal. Urine analysis was negative. He could concentrate urine to 1031; 40 per cent of the dye was eliminated in fifteen minutes. The urea clearance was 40.12 cc. The intravenous pyelogram was normal. The basal metabolic rate was +7 per cent. Under sodium amytal the blood pressure dropped to a minimum of 120/65.

*Operations*—Operations were done on March 18, 1941, and April 1, 1941. Convalescence was uneventful except for a transitory left hydropneumothorax. When the patient left the hospital the blood pressure was 120/74 lying down, 120/70 sitting, and 95/55 in the standing position. No renal biopsy is available.

*Course*—Six weeks after discharge the blood pressure was 118/78 sitting and 106/78 in the standing position. He felt better but had not yet returned to work. Two and one-half years later the blood pressure was 133/92, 130/90, and 142/94 in the three positions. He had no symptoms and worked a full day.

*Comment*.—Based on the early juvenile type of markedly fluctuating blood pressure, on the prominence of nervousness, tremor, and a single elevated metabolic rate, which was found normal at a later date, the diagnosis of a "neurogenic" or perhaps pituitary type of hypertension might be hazarded. The indifferent response to splanchnic section is a further indication in our minds that the mechanism of the hypertension may not be mediated by the splanchnic nerves.

CASE 3—D. T., a 46 year old housewife, entered St. Luke's Hospital on Jan. 22, 1942, complaining of dyspnea on exertion, palpitation, nervousness, cold extremities for five years and severe occipital headaches for six months.

*Past History.*—The patient had had scarlet fever at the age of 5 years. She had 3 pregnancies with two abortions. An elevated blood pressure was noticed after the fourth pregnancy in 1933. A thyroidectomy was done in 1936. Menopausal symptoms have been noted in the past two years. Blood pressure was 160/90 in 1933, 176/96 in 1934. In the past two years she had received theelin, which reduced the blood pressure slightly.

*Intance.*—At time of admission, pressure was 192/104. Eye grounds revealed moderate angiospasm, tortuosity, and nicking of the veins. A soft systolic murmur was heard at the apex. The heart occupied 49 per cent of the thorax; electrocardiogram revealed minor changes. The basal metabolic rate was -4 per cent. The intravenous pyelogram showed a freely movable right kidney with slight hydronephrosis and somewhat delayed function. The left kidney seemed normal. The phenol-sulfonphthalein excretion was 33 per cent in fifteen minutes. Concentration dilution tests ranged between a specific gravity of 1.025 to 1.004 of the urine. The urea clearance was 69.0 standard. Blood chemistry was within normal limits. Cholesterol was 260 mg per 100 cc of blood. Sodium amylal depressed the pressure from 178/96 to 109/70. The cold pressor test raised it from 186/90 to 190/100. Epinephrine raised it from 160/85 to 175/83. On bed rest the pressures varied between 210/99 and 130/70. She was quite emotional and had hot flashes.

*Operations.*—Operations were performed on Feb. 2, 1942, and March 9, 1942. She was discharged on March 17 with blood pressure of 156/86, 142/84, and 69/33 in the three positions. Renal biopsy showed focal, hyaline fibrous thickenings of the glomerular tufts and moderately thickened muscular walls of the arteries.

*Course.*—Four months after operation the blood pressure was 200/110 in the horizontal and 150/100 in the vertical position. She was just as anxious and unstable as ever. On examination for the extent of the denervated area, lack of sweating was complete from the ninth dorsal to the first lumbar on the left and from the tenth dorsal to the second lumbar on the right side. She was placed on small doses of stilbestrol which she had been taking before. She was heard from twenty months postoperatively when the blood pressure was 182/102 lying down, 174/104 sitting, and 170/100 standing. She did a full day's work, but flushes and dizziness were present.

*Comment.*—This patient's blood pressure had fluctuated markedly for many years. She had a thyroidectomy for "nervousness" and tachycardia. She responded only very slightly to epinephrine and to cold as if the vasospasm had been continuous. On one occasion, when a sham injection of saline solution was given preoperatively, her blood pressure was 150/85 when she stated that her blood pressure was going up, her face was warm, and that she knew her pressure was very high. When nurses took the pressure, it was always 20 to 30 points lower. It was felt preoperatively that a severe psychoneurosis was present, but treatment directed toward this factor did not lower the blood pressure.

Technically the operation was complete; the immediate postural hypotension was marked and the area of denervation was satisfactory. One is forced to conclude that the mechanism increasing peripheral resistance was not mediated through the splanchnics. The renal damage was slight and patients with much more severe damage responded well. While we have no hormonal assays one is forced to suspect the pituitary mechanism, either through the antidiuretic or the adrenotropic principle.<sup>1201</sup> Pituitary irradiation was suggested but not carried out. Adequate simple clinical tests for this type of hypertension are

**CASE 4.**—F. F., a 39 year old telephone test man, was admitted to St. Luke's Hospital on Jan. 27, 1912. The hypertension had been discovered only two months previously during a routine physical examination. The only symptom consisted of occipital headaches on rising.

**Past History.**—Past history was noncontributory. The dull occipital headache started around Christmas, 1911. He did not respond to adequate doses of potassium thiocyanate.

**Entrance.**—The patient's blood pressure was 220/120. Physical examination was essentially negative. Eye grounds revealed marked angioma with occasional pin point hemorrhages and scattered small exudates (grade 3 retinopathy). Heart was normal in size. Electrocardiogram revealed no significant changes. The intravenous pyelogram revealed a large right and a smaller left kidney with some hydronephrosis on the right. Both pelves were intrarenal. However, the retrograde pyelogram revealed no obvious pathologic changes; the dye appeared at the left ureter in less concentration than on the right. The urine contained no pathologic elements. Concentration dilution test varied between 1013 and 1.001. The urea clearance was 45, standard. Sugar tolerance was normal and roentgenograms of the sella turcica revealed no pathologic changes. Blood chemistry was within normal limits. Sodium amytal depressed the blood pressure 185/112 to 166/116, intravenous sodium pentothal from 195/130 to 150/115. Epinephrine given intravenously changed the pressure from 174/103 to 210/90; the cold pressor response raised it from 175/114 to 188/122.

**Operations.**—On March 11, 1912, a right sided splanchnic nerve section and dorsal sympathectomy from the ninth to twelfth dorsal were done. There was continuous oozing throughout the operation and patient's condition was so unsatisfactory that the section of the lumbar chain was postponed. Eight days later the right lumbar chain was sectioned below the third lumbar and above the first lumbar, the previous stump of the chain being recognized. The right kidney seemed normal in size, color, and consistency. A small biopsy was taken which revealed normal glomerular tufts and the usual convoluted tubules. Occasional slight hyaline thickening and moderately cellular tubular linings were observed. The blood vessels seemed normal. The biopsy was graded as 0-1. On March 28, 1912, the left splanchnic nerves were excised, together with the chain from the ninth to the twelfth dorsal. Again the patient's pressure fell to low levels under the anesthetic, there was much capillary oozing. The kidney and adrenals, as on the right, seemed normal. The dorsal sympathetic chain seemed unusually large in comparison with the slender splanchnic nerve.

**Course.**—On discharge, the blood pressure was 172/115, 170/120, and 146/110 in the three positions. The patient was free from headaches for a while. One and one half years after operation the blood pressure was 170/120. He was working full time. Following this he was placed again on potassium thiocyanate, to which he responded, while being resistant to the drug before the operation. Two and one half years after operation he is working full time, and while on the drug the blood pressure stays around 160/105.

**Comment.**—The noteworthy facts about this case are resistance to thiocyanate, resistance to heavy doses of barbiturates in the preoperative tests, poor response to the cold pressor test, marked fall in blood pressure and venocapillary oozing under general anesthesia, in spite of advanced retinal changes, a practically normal renal biopsy, and failure of the operations to lower blood pressure in any position. It might be objected that the lack of postural hypotension is due to the nonremoval of the left lumbar chain; however, with the total excision of both splanchnics and the removal of the right chain from the ninth dorsal to the third lumbar, some hypotension is observed at least immediately after the operation.

One is forced to conclude that this hypertension is nonrenal in origin and not one that is mediated to any extent through the splanchnic nerves. If it is diencephalic, it may still be activated through the pituitary gland. Hormonal studies in such cases are sorely needed.

## THE RENAL GROUP

It should be made clear that we are not discussing patients suffering from clinically obvious glomerulonephritis or pyelonephritis. The patients whom we have grouped under this heading are those who are customarily classified as having essential hypertension, that is, there are no, or minimal, urinary findings and the renal functional impairment is commensurate with the duration of a chronic, slowly progressive hypertension. But the history correlated with the renal biopsies allows us to recognize individual characteristics in these groups.

**UNILATERAL HYPOPLASTIC KIDNEY**—It is well known that removal of small hypoplastic kidneys of congenital origin, or those which have atrophied because of a chronic unilateral pyelonephritis, may relieve hypertension. Goldring and Clasis<sup>14</sup> have collected seventy-six published cases in which unilateral nephrectomy was done for high blood pressure. Of these, only seven patients (9 per cent) had a return of blood pressure to normal for a period of two to five years. Personal experience with two children and one adult who were seen in the malignant phase of the disease indicated to us the great importance of recognizing the congenital hypoplastic kidneys early by taking blood pressure readings routinely in children. In previous publications<sup>15</sup> we have reported such cases. We wish to present, however, the type of case which is far more apt to be encountered and in which nephrectomy proved to be unsuccessful and splanchnic section beneficial.

## CASE REPORTS

**CASE 5.**—M. H., a 34-year old housewife, was admitted to St. Luke's Hospital on May 4, 1942, complaining of nervousness, fatigue, dizzy spells, and headaches of ten months' duration.

**Past History.**—There was a negative family history and no past illnesses of significance. Ten months before, while at work, the patient had a sudden attack of fullness in the head, dizziness, and desire to shriek. This spell subsided and blood pressures of 220 to 180 systolic were observed. She was treated with high doses of vitamin A, theelin, and sedatives. She had two uncomplicated pregnancies. Seven years previously, while at a hospital for the removal of a benign tumor of the breast, a normal blood pressure was observed.

**Entrance.**—Blood pressure was 200/120. Eye grounds revealed some angiospasm. The heart occupied 42 per cent of the thorax. Electrocardiogram showed myocardial pathology. Basal metabolic rate was -3 per cent. The intravenous pyelogram revealed a normal left kidney as to size, shape, and position. The right kidney, however, was small and indistinct, giving the impression of atrophy. The retrograde pyelogram confirmed the diagnosis of a small, hypoplastic kidney. The dye appeared at 3 minutes from each ureter, in excellent concentration. The urologic consultant advised right nephrectomy.

The urea clearance was 407 (standard). Concentration dilution varied between 1020 and 1004. The dye was excreted in fifteen minutes, up to 25 per cent. Sodium amylal depressed the blood pressure from 210/124 to 150/100, immersion into ice water raised it from 210/125 to 250/140; epinephrine 1:100,000 raised it from 200/125 to 260/130 and produced the symptoms she complained of.

**Operations.**—On May 11, 1942, the right kidney was explored. It was small, firm, and nodular, and had a coarsely scarred reddish surface. Since the other kidney was hypertrophic and well functioning a nephrectomy was done. No attempt was made to do a complete splanchnic section at this time, but the major splanchnic nerve was clipped and cut for later identification below the diaphragm. Convalescence was complicated by pneu-

mothorax on the same side and atelectasis on the other side. Histologic examination of the right kidney revealed a double pelvis with smooth linings. There was marked nephrosclerosis with local scars.

**Course**—She was discharged with a pressure of 163/100 in the horizontal position and was readmitted on Sept. 26, 1942. She felt well after the nephrectomy, but the blood pressure rose again to 194/110. The heart was enlarging. Blood chemistry was normal. On July 29, 1942, the left splanchnic nerve was cut from the seventh dorsal segment to the celiac ganglion and the dorsolumbar chain was excised between the tenth dorsal to below the first lumbar. She left the hospital with a blood pressure of 128/90, 120/110, and 98/88 in the three positions. Sixteen months later the blood pressure was 185/130, 170/124, and 160/120 in the three positions. She had no headaches, palpitation, or dizziness and worked eight hours daily at manual labor. Since the right splanchnic nerve was never excised, she was urged to have this operation, but was unwilling to do so because of lack of symptoms and ability to work. Twenty-eight months later the blood pressure fluctuated between 165/110 and 150/100. She is considering operation.

**Comment**.—This is a significant history, because it indicates that in spite of a right-sided hypoplastic kidney, nephrectomy was ineffective and left splanchnic nerve section was more helpful. It emphasizes the point repeatedly made in the literature that nephrosclerosis develops in the opposite kidney which will maintain hypertension. Early nephrectomy, however, may produce a cure of hypertension even in the malignant phase<sup>18</sup> with results lasting from three to five years.

**CASE 6**—J. M., 7-year old girl, entered St. Luke's Hospital on Oct. 15, 1937, because of increasing spells of nausea, vomiting, and headaches.

**Past History**—A year previous to entrance, following a choking spell, albuminuria was discovered. Nausea, vomiting, headaches, and restlessness followed a few months later. In June, 1937, she began to have convulsions, with blurred vision lasting two to three days. She had been in bed since that time. Just before entrance she had a series of convulsions.

**Entrance**—The child's blood pressure was 190/160. She had a right-sided facial paralysis and was in a comatose state. She received 50 per cent magnesium sulfate and 5 per cent glucose intravenously. Epistaxis and bloody stools were observed. In the next two days her condition greatly improved so that more detailed study could be started. Eye grounds showed bilateral papilledema, retinal hemorrhages, and exudates. Blood pressure fluctuated between 240/190 and 200/150. It dropped to 190/160 on one third tablet of nitroglycerin. Removal of 50 cc. of blood would also result in the same lowering of blood pressure. The urine contained hyaline and granular casts, there were 50 mg. of albumin in the urine; 55 per cent of the phenosulfonphthalein dye was excreted in two hours. Concentration dilution test showed a variation of specific gravity between 1.011 and 1.014. The urea nitrogen was 49.8; the total nonprotein nitrogen 75 mg. per 100 cc. On a flat plate the left kidney was definitely much smaller than the right. This was confirmed by perirenal air injection.

**Diagnosis**.—The diagnosis was malignant hypertension due to a unilateral renal disease. The patient was discharged but reentered on March 7, 1938, in coma. After a critical period she died one month later. Autopsy was refused.

**Comment**.—This patient was said to have had symptoms for only five months prior to admission. When she arrived at St. Luke's Hospital, and at the time surgical consultation was asked, she was regarded as inoperable because of the high nitrogenous retention. The diagnosis among previous pediatricians was said to be chronic glomerulonephritis. However, unilateral renal disease, amenable to nephrectomy in the earliest, and bilateral splanchnic section in the later stages, was suspected and confirmed by x-ray studies. Whether pyelone-

phritis or congenital aplasia of the kidney was present could not be determined without autopsy.

**CASE 7**—P. B., a 7 year old child, entered the Research and Educational Hospitals on Nov. 27, 1939, on the pediatric service, with complaints of headache, wobbly gait, hematuria, and facial paralysis of several months' duration.

**Past History**—The patient appeared to be a healthy, normal infant until about the age of 1 year, at which time she began to have bouts of nausea and vomiting which persisted until admission. There was hematuria, and swelling of the eyelids occurred four to five times in the last twelve months; frequent severe headaches and uncertain gait developed in the last six months. Two months prior to admission the patient suddenly exhibited a right facial paralysis. Since that time the parents also noted dyspnea on exertion, palpitation, and nocturnal dyspnea.

**Entrance**—The following positive findings were noted: the blood pressure varied from 226/150 to 189/160 mm. of mercury. There was a right facial paralysis. The right pupil reacted sluggishly to light. The right internal rectus muscle was paretic. The right optic disc was slightly elevated. There was a fan shaped hemorrhage on the nasal side of the right retina. The left optic disc was slightly blanched with one pin point hemorrhage. There was angiospasm. The two meter chest film showed enlargement of the heart to the left; the electrocardiogram revealed questionable evidence of myocardial damage. The urine analysis showed a 3+ albumin. The urine culture showed staphylococci, streptococci, and *Bacillus coli*. The nonprotein nitrogen varied between 31 and 40 mg. per cent. Urine could be concentrated to a specific gravity of 1.020. The phenolphthalein dye excretion amounted to 70 per cent in two hours. Urea clearance was 18.7 c.c. per minute (24.8 per cent of normal). The intravenous pyelogram showed no concentration of the opaque solution at 10, 20, 30, and 60 minutes. The retrograde pyelogram revealed pyelectasia and dilatation of ureters bilaterally. The spinal tap showed normal chemistry and pressure.

**Operations**—On Jan. 30, 1940, a left splanchnic nerve section and removal of the sympathetic ganglionated trunk from the twelfth dorsal to the third lumbar were done. The left kidney showed fetal lobulations. A biopsy was taken, the kidney was decapsulated, and an omental graft was wrapped around it. On Feb. 16, 1940, section of the right splanchnic nerve was done, the kidney was scarified, and a muscle flap sutured into it. On Aug. 6, 1940, a right lumbar sympathectomy from the twelfth dorsal to the third lumbar completed the operation. The postoperative blood pressure was 140/136, 170/130, and 175/140 in the three positions. The patient was asymptomatic after the last operation.

The renal biopsy revealed one portion of the section containing normal glomeruli tubules and interstitial tissue. The lumens of the arterioles were exceedingly small, because of intimal proliferation. There was some recanalization of partially obliterated arterioles. The arteries had hyperplastic media but the lumina were of normal caliber.

In another portion the tissue resembled fetal thyroid; these were undoubtedly remains of kidney tissue since renal tubules were unmistakable. Islands of dense fibrous tissue surrounded delicate tubules with cuboidal epithelium. Some of the tubules were filled with a hyaline-like material. Some of the arteries and arterioles had no lumen being replaced by dense fibrous tissue. The entire picture was consistent with embryonic renal structures with arteriolar obstruction secondary to hypertension.

**Course**—The patient was asymptomatic from August, 1940, to November, 1941, at which time she was re-admitted because of recurrent headaches, vomiting, strabismus, burning on urination, dizzy spells, and ataxic gait, all of two weeks' duration. Blood pressure was 190/150 in all positions. The urine culture yielded *Bacillus coli* and *Streptococcus faecalis*. Albumin was 1+, and there were occasional red and white blood cells in the urine. The urea clearance was 23.7 c.c. per minute. The patient developed mumps and scarlet fever and was transferred to Cook County Hospital.

On March 19, 1942, two years postoperatively, the patient was readmitted to the pediatric service complaining of recurrent attacks of facial paralysis. The blood pressure varied from 240/250 to 190/110. The arteriovenous ratio in the eye grounds was 1:4 to 1:5; there

were silver wire arteries and old retino optic hemorrhage. The urine showed a 4+ albumin (about 3 to 3.5 Gm daily). There were occasional hyaline and granular casts. She could concentrate urine only to 1013. Nonprotein nitrogen was from 50 to 72 mg per cent. The urea nitrogen was 73.3 per cent, and creatinine 2.3 mg per cent. The electrocardiogram showed only slight deterioration as compared with the one obtained in 1940. She was discharged on April 5, 1942, with a diagnosis of malignant hypertension with impending uremia.

*Comment.*—This 7-year-old child was operated on in 1940, for bilateral congenital hypoplastic kidneys resulting in a malignant phase of hypertension. She had papilledema and retinal hemorrhages, and did not respond to vasodilators except mecholyl. Her subsequent course downhill, which perhaps was not as rapid as it might have been if she had not been operated upon, showed a gradual progression of the renal damage to terminal uremia. The onset of the lesion and the findings of the biopsy leave no doubt that a congenital hypoplasia of renal tissue was responsible for the hypertension. At the age of 7 years, when the condition was first recognized, the hypertension was in a malignant phase and inoperable according to our present indications. Nephrectomy was not feasible, first because both kidneys were involved with a superimposed pyelonephritis and second because the arteriolar lesion had injured the other kidney. Certainly a recognition of such a lesion at the age of 1 or 2 years instead of at the age of 7 might have given this child a better chance.

**HYPERTENSION FOLLOWING RENAL TRAUMA**—Two patients in this series had a history of severe trauma to the region of the kidney, followed by hematuria, and exhibited deformed renal calices or decrease in the size of the kidney. Whether the trauma is a factor in their hypertension is debatable. However, we have grouped these two patients together, since their history and their reaction to surgery was so similar.

**CASE 8.**—J. A., a 31 year old grain dealer, was admitted to St. Luke's Hospital on May 19, 1943, stating that he knew of his high blood pressure, however, he had no symptoms referable to it.

*Past History*—In high school he had been kicked in the right flank after which he went into shock and had blood in the urine. About ten years before entrance he suffered from malaria for two years. Five months before entrance, on physical examination from the Army, he was told that he had a blood pressure over 200 mm of mercury. Local physicians had obtained pressures between 200 and 150 mm. of mercury. His mother had died at 60 years of age of a stroke; his father had died at 56 of a heart attack, one brother, aged 52, had high blood pressure.

*Entrance*—The patient's blood pressure was 210/134. Physical examination revealed a diffuse enlargement of the thyroid gland, especially on the left. There was a soft systolic murmur at the apex and an occasional faint splitting of the first sound. The eye grounds showed moderate spasm of the retinal arteries with some arteriovenous compression; the retinopathy was grade 2. The heart occupied 59 per cent of the thorax; the left ventricle seemed slightly enlarged. Electrocardiogram showed evidence of myocardial damage with the first and second thoracic inverted, the third thoracic low and the ST segment elevated in Lead IV. The basal metabolic rate was -8 per cent. The intravenous pyelogram revealed some dilatation of the ureter, sharply localized just below the sacroiliac joint and the displacement of the right ureter in its mid portion toward the midline. The urine was negative. The kidneys concentrated from 1003 to 1024. The urea clearance was 82.5 cc (standard). Blood chemistry was normal. The response to ice water was from 194/136 to 240/150 mm. of mercury; sodium amylal depressed the blood pressure from 172/131 to 140/100.



**Operations**—Operations were done on May 26, 1943, and Oct. 11, 1943. Since he had a stitch abscess after the right splanchnic nerve section, he was discharged and the left side operated on five months later. Blood pressure, six months after the completion of the second operation, was 140/103, 150/103, and 145/103 in the three positions. The specific gravity of the urine was 1.030. He was asymptomatic, but after one week of steady drinking the pressure was 180/110. One year after the completion of the second stage the blood pressure was 130/84 in all positions. Two years after the operation he was asymptomatic, working full time, with a blood pressure of 120/80 mm. of mercury.

**Comment.**—This patient had a bad family history; whether the trauma to the right kidney accelerated the appearance and progress of the hypertension is open to debate. The vasomotor reactivity was exaggerated. He had kinks in both ureters, perhaps due to strictures and early pyelonephritis. The combination of these factors, however, produced a severe hypertension in a man of 31 years, the operation up to the time of this report has been definitely beneficial. Note that the preoperative basal blood pressure (under 9 gr. of sodium amytal) corresponds to the postoperative pressures at six months, but that he continued to improve later.

**CASE 9**—L. F., a 17-year-old boy, entered the Research and Educational Hospitals on Aug. 13, 1941, complaining of occasional frontal headaches, fatigue for the past eighteen months. An elevation of blood pressure was discovered four months before.

**Past History**—The patient had an injury to the right side at the age of 9 years, resulting in internal hemorrhage and hematuria. He had always been active; one grand mother had hypertension.

**Examination**—Physical examination was negative except for a blood pressure of 180/120. The eye grounds revealed slight anisotropia. The electrocardiogram showed changes compatible with left heart strain. The heart in the two meter chest film occupied 50 per cent of the thorax. The urinalysis showed an occasional red blood cell, cast, and slight albuminuria. The urea clearance was 58 c.c. (maximal). The phenol-sulfonphthalein dye appeared in 40 per cent concentration in fifteen minutes. Concentration was possible to 1:025. The insulin clearance was 118 c.c.; the diolact clearance was 574 c.c. per minute. The pyelogram showed an unusual deformity of the right renal pelvis. Blood chemistry was within normal limits. Ice water raised the blood pressure from 180/120 to 210/140. Sodium amytal depressed it from 210/110 to 108/100 mm. of mercury. Epinephrine raised it from 212/138 to 300/176 mm. of mercury.

**Operations**—Bilateral dorsolumbar sympathectomy and splanchnic nerve sections were done on Jan. 13, 1943, and Oct. 11, 1943. On discharge the blood pressure was 132/90, 130/90, and 90/50 mm. of mercury.

**Course**—Three months later the blood pressure was 150/100, 130/90, and 120/80 mm. of mercury. There were no complaints. Six months later the blood pressure was 150/100, 142/90, and 148/90 in the three positions. He was working full time and felt well. One year later the pressures varied between 140/90 and 124/84 mm. of mercury in the horizontal position. Electrocardiogram showed improvement compared with the preoperative one.

**Comment**—Again there is increased vasomotor reactivity, history of a renal injury, and severe juvenile hypertension. The blood pressure under sodium amytal was 168/100 before the operation; the blood pressures six months following operation were from 150/100. One year after the operation the blood pressure was 140/90. Three years after the operation the blood pressure was 135/90.

**POST-TOXEMIC HYPERTENSION.**—Our present knowledge concerning pre-eclamptic and eclamptic toxemia of pregnancy has been summarized and extended

by the monograph of Dexter and Weiss.<sup>17</sup> We quote. "Sustained hypertension follows toxemia of pregnancy in about one-quarter of the patients who had normal blood pressure before pregnancy. It is not so much the severity but the duration of the toxemia which is responsible for the persistent hypertension."

The main histologic changes are found in the placenta, liver, kidney and retina. Renal changes specific for toxemia were described by Fahr as glomerulonephrosis.<sup>18</sup> There is evidence that in toxemia a generalized damage of the capillary endothelium exists. The clinical effect of this is a type of hepatorenal syndrome with cerebral manifestations.

The renal lesion secondary to toxemia is an example of a state in which endogenous factors, such as originate in the placenta, liver, or glands of internal secretion, produce structural arteriolar changes in the kidney which in turn may produce renal ischemia and the liberation of pressor substances producing hypertension. It would seem that the incidence of post-partum hypertension may be greatly curtailed by not allowing toxemia to persist more than three weeks during pregnancy.

Some of the case histories to be presented are a sad commentary on the indifference or carelessness of some obstetricians. If the toxemic injury to the kidneys lasts too long, or if repeated toxemias are allowed to persist, a malignant hypertension may be the result. But with a single injury, which subsides and does not continue to damage the kidney, the results have been very favorable. The resulting nephrosclerosis yields to our surgical approach and some of our best results have been in patients with grade 2 hypertension of this group.

**CASE 10**—A. S., a 33 year old housewife, was admitted to Research and Educational Hospitals on March 2, 1942, complaining of dyspnea on exertion, frequent headaches, dizziness, precordial pain on exertion, and palpitation for the past twelve months.

**Past History**—The patient was told of an increase in blood pressure one year before, when she was in the seventh month of pregnancy. Previous pressures were normal. She was placed at bed rest until after delivery, which was normal. She had two previous uncomplicated pregnancies. Her mother had died in the early forties of high blood pressure.

**Entrance**—Blood pressure was 166/110 mm. of mercury. Physical examination was essentially negative. Eye grounds revealed angiospasm of retinal vessels with an arterio-venous ratio of 1:4 and slight nicking. Heart was moderately enlarged on x ray examination. Basal metabolism was +9 per cent. Concentration of urine was possible to 1070. The phenol-sulfonphthalein dye was excreted up to 30 per cent in fifteen minutes and 59 per cent in one hour. Urea clearance was 48 per cent (standard). The intravenous pyelogram was normal. Sodium amylal depressed the blood pressure to 122/80 mm. of mercury, ice water raised it from 140/100 to 160/122 mm. of mercury.

**Operations**—Operations in two stages was done on April 14 and 28, 1942. On discharge the pressure was 142/96, 128/92, and 84/56 in the three positions.

**Course**—One and one half years later she complained of an occasional headache, no dizziness or fatigue. The headaches were premenstrual. She worked all day. The pressure was 120/85, 118/85, and 122/85 mm. of mercury in the three positions. Two and one half years later the pressure was 120/80 in all three positions.

**Comment**—The toxemia in this patient lasted for the last two months of pregnancy. The post-toxemic hypertension had persisted for only one year before operation. The vasomotor relaxation resulted in a normal blood pressure.

Under such favorable conditions a restoration of blood pressure to normal was accomplished. Further pregnancies should not be permitted.

**CASE 11**—M. C., a 33 year old married woman, entered St. Luke's Hospital on Dec. 15, 1940, complaining of hives and edema of face, wrists, and ankles since the age of 17, headaches, dizziness, and palpitation of at least twelve years' duration.

**Past History**—The patient had had emotional urticaria and edema since the age of 17. They were not demonstrably caused by foods, cosmetics, or seasonal variations. In 1928, during the first pregnancy, hypertension was discovered. She had a great deal of nausea, vomiting, and edema, and in the eighth month she had nine severe convulsions with anuria for four days. A cesarean section was performed and a dead infant delivered. She seemed fairly well until 1933 when following a "head cold," nausea, vomiting, and generalized edema returned. Again she was anuric. In 1936 the headaches stopped. During the last few months before admission she felt increasingly fatigued, sleepy, and noticed dizziness on walking.

**Entrance**—The fundi showed arteriolar spasm, arteriovenous nicking but no retinal hemorrhages or exudates. The blood pressure varied from 210 to 140 systolic and 140 to 90 diastolic. The lowest pressure under sodium amytal was 172/88. The cold pressor test raised the blood pressure from 150/100 to 186/110 mm. of mercury. The heart occupied 53 per cent of the thorax. Electrocardiogram showed minimal myocardial damage. The basal metabolism was +9 per cent. Urea clearance, concentration dilution, and phenolsul fophthalein elimination were within normal limits. A diagnosis of postclampsic hypertension, grade 1, was made.

**Operations**—Operations were performed on Dec. 16 and 28, 1940. A bacillus coli pyelitis followed the second stage. Renal biopsy revealed chronic glomerular, tubular, and interstitial damage. She was discharged with a blood pressure of 114/80 in the horizontal position.

**Course**—The patient began to gain weight. The previous restlessness disappeared. Postural hypotension (60/0) was marked for six weeks, after which it caused no complaints. It was absent after three months. Up to thirty six months after operation the blood pressure varied from 120 to 105 systolic and 86 to 75 mm. of mercury diastolic pressure. At the last examination, three and one-half years after the operation, blood pressure was 150/90, 140/100, and 120/84 in the three positions. However, she suddenly lost her eyesight and a tentative diagnosis of cerebral aneurysm at the base of the brain was made.

**Comment**—This patient had a history of toxemia of pregnancy with convulsions, she also had a marked vasomotor instability as manifested in the emotional urticaria and edema. An excellent control of blood pressure was obtained for three and one-half years, whether the vascular lesion at the base of the brain is a congenital or an arteriosclerotic weakening of the vessel wall is impossible to determine. At this time she is almost completely blind, with a normal blood pressure. The symptoms date back twelve years.

**CASE 12**—K. de T., a 30 year old housewife, was admitted to St. Luke's Hospital on June 22, 1941, complaining of severe headache and dyspnea on exertion for two years. She had an attack of numbness on the entire left side with inability to walk which lasted one to three days, ten months previous to entrance.

**Past History**—Ten years previously she had a toxemia of pregnancy. The pregnancy was not terminated and she has one healthy child. Her blood pressure was normal before and during the first trimester of pregnancy. Her mother had died in an uremic state and her father had died of a stroke.

**Entrance**—The patient's blood pressure was 200/120 mm. of mercury. Physical examination was essentially negative. Eye grounds revealed a generalized arterial constriction with an occasional white exudate. The heart occupied 46 per cent of the thorax; the

electrocardiogram showed no diagnostic deformities. She concentrated and diluted urine between 1019 and 1002; the dye was excreted to 10 per cent in fifteen minutes. Urea clearance was 59.4 c.c., blood chemistry was normal as was the intravenous pyelogram. Sodium amytal depressed the blood pressure from 196/122 to 166/118 mm. of mercury. Ice water raised the pressure from 189/123 to 236/170 mm. of mercury.

**Operations.**—Bilateral dorsolumbar sympathectomy and splanchnic nerve section were done on June 27, 1941, and July 11, 1941. The kidney felt hard and small, and whitish scars were on its surface. The second stage was followed by pneumothorax and pleural effusion, but no delay in convalescence. She left the hospital on July 27, 1941, with the following blood pressure: lying down, 115/100, sitting up, 90/60, standing, 80/0. The renal biopsy showed hyaline, shrunken glomeruli, thickened vessel walls, a marked nephrosclerosis.

**Course.**—The patient was re-examined every three months the first, every six months the second year. On Nov. 15, 1943, two years postoperative, the pressure was 160/115 in the horizontal, 140/110 in the sitting, and 130/110 in the standing position. Urine showed no pathologic elements; the specific gravity was 1015. She had no headaches or dizziness, had occasional palpitation, but felt very listless. On April 11, 1945, the pressure rose to the preoperative level.

**Comment.**—This patient had a normal blood pressure before pregnancy. Family history for cardiovascular renal disease was unfavorable. She had generalized edema in the fifth month of pregnancy. She was operated on for a grade 2 hypertension with irreversible renal damage, with poor response to barbiturates, and an excessive response to ice water. Four years after operation both the symptoms and the actual blood pressures were close to where they were prior to operation. While she had four years of comfort and the process seemed to have been arrested, there is now a recurrence of the hypertensive state. In retrospect the following observations might point to such a course: (1) Under sodium amytal the minimum pressure obtained was 166/118, the diastolic being somewhat higher than we like it to be; (2) the concentration test showed values up to 1019, the phenolsulfonphthalein excretion in fifteen minutes was only 10 per cent. On the other hand, the urea clearance was comparatively high—59.4 c.c.; (3) during anesthesia the blood pressure did not drop very much and stayed around 160/120, indicating as the operative note stated that "organic damage was considerable"; (4) inspection and palpation of both kidneys revealed small, hard, shrunken kidneys showing small white depressed scars on the surface.

In addition, the patient's married life had been unfortunate, ending in divorce and remarriage. She was restless, unhappy, and had avoided all responsibility in both of the marriages. The last examination almost four years after the operation revealed a recurrence of symptoms and return of the blood pressure levels to a slightly lower than preoperative level. One lumbar chain was not completely severed. The renal damage was too great. These two factors were held responsible for the recurrence.

**CASE 13.**—H. F., a 23-year-old housewife, was admitted to St. Luke's Hospital on May 11, 1912, complaining of nervousness for six years; severe headaches for two years; "strokes" one and two years before admission, with transient aphasia and paralysis of left and right upper extremity for four to six weeks each time; redness of lower extremities and occasional hematuria.

*Past History*—The patient was perfectly well until six years before when she became very nervous. Five years before she had a severe toxemia of pregnancy with convulsions and generalized edema for the entire third trimester. The infant was stillborn. While the patient had scarlet fever at the age of 9, which left her with a discharging ear, she had no kidney trouble and the blood pressure was not elevated before the pregnancy. The family history was not contributory.

*Entrance*—The patient's blood pressure was 135/90 mm. of mercury. Physical examination revealed a slight left lumbar tenderness and residual weakness and epusivity of both arms and hands. There was left facial weakness. Eye grounds revealed a slight bitemporal pallor of the discs. The heart occupied 42 per cent of the thorax; electrocardiogram showed evidence of myocardial damage. She concentrated urine to 1,022 and diluted to 1,002; excreted the dye to 20 per cent in fifteen minutes. The uric clearance was 144 cc. (standard). There was persistently more than 50 mg of albumin in the urine. The intravenous pyelograms were normal, but there were some calcified spots to the right and left of the midline suggestive of calcification in the suprarenal glands. There was some old infiltration in the upper portion of the right lung, which appeared to be well organized. Sodium amytal depressed the blood pressure from 130/94 to 100/80 mm. of mercury. On immersion into ice water the pressure rose from 135/90 to 140/96; epinephrine raised the blood pressure from 130/90 to 190/100 mm. of mercury. The impression was that of a postleptemic hypertension resulting in diffuse arteriolar disease. The diastolic pressure was consistently above 90 mm. of mercury, but the systolic was low owing to myocardial damage or possibly damage to the adrenal glands.

*Operations*—Operations were performed on May 20, 1942, and June 8, 1942. Following the first stage the patient exhibited a temperature of 104.6° F., a slow pulse and respiration, and a marked mottled peripheral cyanosis. This was thought to be a cerebral vascular accident in the midbrain or a Waterhouse-Friderichsen syndrome which fortunately subsided in three days. The second stage was performed nineteen days after the first one without any unusual complication. The kidneys were small and firm and both adrenals were also visualized; while the adrenals felt smaller and more nodular than normal, there was no evidence of tumor or calcification on palpation. The renal biopsy taken from the right kidney showed marked fibroplastic changes, there were wedge-like sections of cellular fibrous tissue, which extended deep into the parenchyma. Here the tubules and glomeruli had undergone marked retrogressive changes. There were clusters of atrophic glomeruli reduced to masses of hyaline material and the tubules had disappeared almost completely. There were also lymphocytes with small residues of tubule cells. There were various stages of involution but outside these wedges the tubules contained columnar lining cells and the lumens were filled with granular precipitates. The glomerular tufts in these portions were also cellular and had considerable fibrous stroma. The large blood vessels included in the scarred portions had very narrow lumens and intimal fibrous tissue thickenings, but the blood vessels elsewhere also had thick muscular walls with some fibrous thickening along the intimal edge. The interpretation of these findings was that nephrosclerosis was the main tissue change.

*Course*—When the patient left the hospital on Aug. 19, 1942, the blood pressure was 112/80. The epinephrine sensitivity decreased. She was re-examined on July 3, 1943, with a blood pressure of 110/70 in the horizontal, 100/70 in the standing position. She felt well and used the paralyzed arm more freely.

*Comment*—This was a frail, constitutionally inferior patient who received a severe vascular lesion during pregnancy. Whether there was a latent adrenal insufficiency present was uncertain and it was not feasible to test her for this. The cerebral, cardiac, and renal lesion might have been embolic in nature originating from a subacute bacterial endocarditis but this suggestion, made by our medical consultant, could not be confirmed or disproved. While the weakness and easy fatigability persist to this day, the blood pressure has remained

TABLE II. CORRELATION OF CLINICAL GRADES OF HYPERTENSION WITH RENAL HISTOLOGY

GRADES	NUMBER OF CASES		REMARKS
	CLINICAL	RENAL	
1	10	14	4 patients with grade 2-3 hypertension had grade 1 renal changes
2	13	9	4 patients differed, the biopsy always showing less advanced changes
3	7	7	1 malignant case had a grade 1 renal biopsy 1 patient with grade 2 hypertension showed grade 3 histologic changes

normal for three years and she can do her own housework. The diagnosis of postelempytic hypertension is still the most likely.

**THE PYELONEPHRITIC HYPERTENSION**—In their monograph on the relation of pyelonephritis to hypertension, Weiss and Parker<sup>10</sup> made the important point that the severity and diffuseness of the vascular lesion in this disease is closely related to the degree of hypertension. Patients with severe hypertension had advanced hyperplastic arteriolosclerosis, productive endarteritis, and necrotizing arteriolitis in the kidney. They also stated that pyelonephritis is responsible for at least 15 to 20 per cent of cases of malignant hypertension.

This is in contrast to many statements in the literature that patients with pyelonephritis do not have a higher incidence of hypertension than those of a similar age group without pyelonephritis. However, such collective statistics miss the evaluation of the individual severity of the lesion, whether the pyelonephritis is acute, chronic, recurrent, or healed. Early in our studies of renal biopsy material it was found that the so-called essential hypertension, with no history and no urinary findings of a pyelonephritis, may reveal a renal histology consistent with a latent or healed pyelonephritis. The differential diagnosis between the vascular changes in pyelonephritis and nephrosclerosis has been discussed in detail in another communication.<sup>3</sup> Here only a table is reproduced (Table III).

CASE 14—A B, a 33 year old housewife, was admitted to St Luke's Hospital on May 20, 1941, complaining of fullness of head and face and weakness for two years, obesity for past few years, and transient edema of eyelids and ankles for the past two years.

TABLE III. DIFFERENTIAL DIAGNOSIS OF VASCULAR LESIONS IN PYELONEPHRITIS AND NEPHROSCLEROSIS

VASCULAR LESION IN	PYELONEPHRITIS	NEPHROSCLEROSIS*
Arteries	Productive endarteritis (basophilic reticular tissue) Reduplication of internal elastic membrane Medial hypertrophy	Internal thickening due to acidophilic, dense connective tissue, and hyalinization Splitting and reduplication of the internal elastic membrane
Arterioles	Concentric proliferation of cells with increase in collagen Hyperplastic arteriolar sclerosis Hyaline degeneration only in the older group	Hyaline degeneration

\*The malignant phase produces changes identical with those seen in pyelonephritis, that is, productive endarteritis and hyperplastic arteriolar sclerosis.  
Based on the monograph of Weiss and Parker.<sup>10</sup>



**Entrance.**—The blood pressure was 220/140 mm of mercury. Physical examination revealed evidence of some recent weight loss, slight emphysema of the chest, and an enlargement of the heart to 1 cm to the left of the mediastinal line. The eye grounds showed an early grade 3 hypertensive retinopathy. An electrocardiogram revealed left ventricular preponderance. The basal metabolic rate was -1 per cent. He was able to concentrate urine to 1038. The phenolsulphonphthalein test showed 25 per cent excretion in the first fifteen minutes. The urea clearance was 47 c.c. (standard). The intravenous pyelogram showed poor filling of the left pelvis. No retrograde pyelogram was done. The urea nitrogen was 19, the nonprotein nitrogen 38, giving a urea ratio of 50. Sodium amylal depressed the blood pressure from 206/124 to 160/114, sodium nitrite from 202/118 to 156/108, and intravenous pentothal from 180/130 to 122/92. Ice water modified the pressure from 188/134 to 172/120, an inverse reaction.

**Operations.**—Operations were performed on Dec. 8, 1940, on the right and three weeks later on the left side. Blood pressure when the patient left the hospital was 160/100 in the horizontal, 154/108 in the sitting, and 102/88 in the standing position. Renal biopsy was reported to be consistent with chronic pyelonephritis.

**Course.**—One month after discharge the patient was able to sleep without sedatives and had only a few headaches. He still had some precordial discomfort. The blood pressure was 180/128 in the horizontal position. Six months later he was back at work with a pressure of 160/100 in all positions. Examined four years postoperatively, blood pressure was 150/100 in all three positions. He could work eight hours daily but felt tired at the end of the day and had occasional headaches.

**Comment.**—Compared with the considerable organic damage which this patient exhibited before the operation, the postoperative course has been quite favorable. This was a grade 2 hypertension originating from a pyelonephritis.

**STREPTOCOCCUS NEPHRITIS FOLLOWED BY HYPERTENSION.**—It is sufficiently known that the nephritis following scarlet fever or streptococcus infections may give rise to a persistent hypertension. That such a nephritic hypertension responds to sympathectomy is illustrated in Case 16.

**CASE 16.**—J. G., a 15-year-old white boy, entered the Research and Educational Hospitals on Feb. 12, 1941. He had no complaints.

**Past History.**—This boy had always been well and had no difficulty other than some social maladjustment. Five years previous to entrance, at the age of 10 years, he had erysipelas of the face complicated by renal involvement. During this time he had blood, hyaline, and granular casts in the urine and the blood pressure rose to 180/120 mm. of mercury. A physical examination done six months before entrance disclosed a blood pressure of 160/100 mm. of mercury for which reason he was referred to the University Clinics.

**Entrance.**—The patient's blood pressure was 175/125 mm. of mercury. The fundi seemed normal. The examination of the heart revealed an old rheumatic mitral valvulitis. The electrocardiogram was consistent with an old rheumatic heart disease. The two meter chest film showed the heart and great vessels to be of normal size. The urine showed an occasional cast and a trace of albumin. The urine could be concentrated to 1,026. The dye was excreted to 30 per cent in fifteen minutes and the urea clearance was 40 c.c. (standard). Sodium amylal depressed the blood pressure from 160/110 to 125/80, the ice water raised it from 145/90 to 160/100, epinephrine raised it from 160/95 to 190/90. On bed rest the lowest pressure obtained was 145/90.

**Operations.**—Operations were performed on June 24, 1941, and July 1, 1941. The postoperative course was uneventful. The blood pressure on discharge was 110/72 lying, 70/50 sitting and 50/38 in the standing positions. Unfortunately no renal biopsy was available.

**Course.**—Two months postoperatively the patient had no complaints of any kind and was working as a waiter. A blood pressure in the sitting position was recorded to be 118/80.



No further visits to the Dispensary are recorded since he was inducted into the Army in the same year (1911). Information received from his father in October, 1943, revealed that he had been on active duty in Alaska for two years and had no complaints. Efforts to obtain a blood pressure reading have so far failed.

*Comment*—The sequence of crysipelas followed by hematuria and hypertension make the diagnosis of a streptococcus nephritis most likely. This may well be a vascular type of sensitization as Andrews, Derick and Swift,<sup>20</sup> and Rich and Gregory<sup>21</sup> have postulated. The effect of splanchnic nerve section on this lesion was gratifying.

**THE RHEUMATIC HYPERTENSION**—In a short, mostly ignored communication Fahr<sup>22</sup> stated that the rheumatic infection may produce a malignant, not arteriolar sclerotic type of nephrosclerosis. In this country the studies of Taussig and Hecht<sup>23</sup> have shed important light on the subject, although neither pediatricians nor internists seem to have recognized the importance of these statistical studies. They first described three cases in which during the course of rheumatic fever hypertension developed under observation, nephritis or other causes of hypertension were excluded. Next they studied the histories of 500 rheumatic children, forty nine of these had hypertension. While they stated that the exact relation between the hypertension and the rheumatic infection was unclear, again no children with nephritis or with other obvious causes for hypertension were included.

We wish to present a few cases from our surgical material and one final one observed on the medical service of the Research and Educational Hospitals which would indicate the comparative frequency of this lesion and their responsiveness to surgical treatment.

**CASE 17**—J. W., a 24 year old white man, entered the Research and Educational Hospitals on April 23, 1942, complaining of weakness, dyspnea on exertion, and palpitation of three months' duration.

*Past History*—The patient had had rheumatic fever at the age of 12 years and associated arthropathy with a recurrence at the ages of 16 and 17. At the age of 19 he showed some ankle edema. In 1941, at the age of 23, he developed another attack which kept him in bed off and on until his entrance to the hospital. There were no other diseases and the family history was negative except for one brother with hypertension.

*Entrance*—The patient's blood pressure was 134/90. The heart was of normal size on physical examination and on a two-meter chest film. There were, however, a palpable thrill and a loud systolic murmur at the apex of the heart. Funduscopic examination revealed a grade 1 hypertensive retinopathy. The electrocardiogram showed the presence of mitral heart disease. The basal metabolic rate was -2 per cent. Blood chemistry was normal. The urine could be concentrated to 1034; 10 per cent of the dye was excreted in the first fifteen minutes. The urea clearance was 27 c.c. (standard). The intravenous pyelogram was normal. The insulin and diolast clearances were within normal limits. Under sodium amytal the pressure dropped from 160/90 to 114/80; sodium nitrite lowered the pressure from 140/90 to 122/80. Ice water raised the pressure from 154/98 to 184/125. Epinephrine raised the pressure from 160/92 to 160/90.

This was a grade 1 hypertension in a 24 year-old individual with rheumatic heart disease and operation was advised.

*Operations*.—Operations were performed on July 14, 1942, and July 23, 1942. The postoperative course was uneventful. On discharge the pressure in the horizontal position was 138/90, sitting 130/90, and could not be obtained on standing. No data were available as to the level of sweating. Renal biopsy showed hyperplastic arteriolar sclerosis and productive endarteritis.

*Course*.—Six months postoperatively the patient was working eight hours a day; he complained of fatigue but less dyspnea. Blood pressure was 140/82 lying down, 140/80 sitting, and 120/80 standing. As a hotel clerk he stood most of the time. One year after the operation blood pressure was 140/80 in all positions; he of course still had the symptoms of not entirely compensated mitral heart disease. Three years after operation blood pressure was 138/80.

*Comment*.—This was a patient with a history of rheumatic infection, a rheumatic heart, and a hypertension of vascular origin showing hyperplastic arteriolar reaction in the absence of pyelonephritis. These findings seem more than coincidental.<sup>23</sup>

*CASE 18*.—J. W. M., a white girl aged 15 years, unmarried, was admitted to the cardiac clinic of the University Dispensary on Oct. 15, 1938 and then to the Research and Educational Hospitals on November 8, 1938 complaining of shortness of breath, palpitation, tremor, nervousness, and weight loss of five months' duration.

*Past History*.—Eight years previously, at the age of 7, the patient had chorea and "heart trouble" which responded satisfactorily to bed rest. She was normally active for the next seven and one half years. Five months prior to entrance she developed a violent attack of palpitation followed later by "trembling." Later a weight loss occurred in spite of an adequate appetite. Two weeks before admission attacks of dyspnea occurred independent of the tremor or palpitation. Her father died of pulmonary tuberculosis at the age of 38. Her mother has an arrested case of tuberculosis, she had had a thoracoplasty.

*Entrance*.—The patient's blood pressure was 168/120 mm. of mercury. The heart was enlarged to the left. The first mitral sound was replaced by a short systolic murmur. The pulmonary second sound was louder than the aortic second. Two meter chest film showed an increase in the hilus shadow with considerable calcification suggesting an old tuberculosis. The basal metabolic rate was 9 per cent. Blood chemistry was within normal limits. Urea clearance was 45 c.c. (standard). The cold pressor test showed a maximum systolic rise of 24 mm., a maximum diastolic rise of 46 mm. of mercury. Intravenous sodium pentothal lowered the pressure from 184/138 to 126/94. She was discharged on Nov. 23, 1938.

*The second hospital admission* occurred on Feb. 20, 1940. Added complaints on this admission included precordial pain and orthopnea for one month. Blood pressure at bed rest was recorded as varying from 140/110 to 158/120. A psychiatric consultation was requested and conferences were arranged.

*Summary of Psychiatric Interviews*.—Psychotherapeutic interviews took place twice weekly from March 23, 1940, to May 23, 1940, a total of seventeen hours. During this period, the patient reported only one nocturnal anxiety attack. Blood pressure readings were made during about half of the visits at about ten minute intervals. The range of systolic pressures was 144 to 174, most of the readings falling between 150 and 160. Even in the presence of acute anxiety the systolic pressure did not rise above 174. The diastolic pressure varied from 108 to 136, the usual readings being between 120 and 130. The systolic pressure was more labile than the diastolic pressure and appeared to fluctuate under the influence of emotion. Thus, when the patient was apprehensive about the material under discussion, the systolic level ascended to the region 170. When her fears were allayed by reassurance, the level fell to 150 or lower. Diastolic pressure, however, remained relatively fixed.

The patient proved to be cooperative in the interviews and showed willingness to deal with the materials brought up by the interviews. Her fear of unrecognized tendencies in her personality made progress slow. From the interviews as well as from a social history obtained from the mother and the sister, an opinion may be ventured about the psychological side of the case. The striking fact is the discrepancy between a sensitive and highly vulnerable make up, and inhibition of expressive feeling. On the one hand the patient had always been easily stirred emotionally, and on the other hand she had never been known to release angry feelings. In working with the materials of her life, one gained the impression that she had stored up an immense amount of hostile feeling; yet, she had the reputation

for being a very gentle and soft spoken person. This contrast was exhibited in her behavior during the interviews. Although appearing calm and well poised, she reacted very sensitively to any remark bearing on her personal problems and obviously struggled for control of her emotions. It seemed that the accumulation of unhappy emotion over the years was related to the hypertension. The energy of the emotion being blocked in expressive behavior, it found an outlet in the vascular system.

The origin of the hostile reactions and of the need to suppress them require rather lengthy discussion for their elucidation. In a word, it may be stated that the hostilities arose out of rivalry with mother and sister and a protective response to the consistently aggressive behavior of the sister. The inhibition of frank emotional response was due to fear of punishment. The latter was associated with many fantasies of punishment animated by experiences of an everyday kind. The constant evocation of these fantasies made expression of emotion dangerous, and filled the patient with anxiety. One of her punishment fantasies was sudden death by reason of heart failure, this fantasy having grown out of the diagnosis "leakage of the heart" made in childhood. It was this fantasy which appears to have been responsible for the anxiety attacks at night. Reassurance on this point may have played a role in eliminating the attacks. Another punishment fantasy consisted of being mutilated. Under the influence of this fantasy, the patient had for years dreaded an operation as a punitive procedure. The impending operation of sympathectomy caused a great deal of anxiety, reflected in the rise of the systolic level to about 200 following admission to the hospital.

The psychotherapeutic aim in this case was to bring about a release of the repressed emotion by removing the fears that blocked its expression. This process of desensitization necessarily required a long period of psychotherapy. During the course of treatment, blood pressure levels sometimes rose as the result of the emergence of fear. Ultimately, however, if the hypothesis of a relationship between hypertension and repressed emotion was correct, release of the emotion should have brought about a lowering of the blood pressure. Even if sympathectomy were successful, the patient should continue under psychiatric care because the emotional tension did not find release in some other healthy mechanism. And apart from the threat to health, the patient required insight and guidance in improving this general adjustment.

*Comment*—There are several reasons for giving this patient's history in more detail. She had a good history and clinical evidence for a rheumatic infection. She seemed to be suitable for sympathectomy since she belonged to group 1. The psychiatric interviews disclosed an interesting light on her personality but the seventeen weekly conferences had no effect on the blood pressure and her renal function had meanwhile deteriorated. Blood pressure became normal after bilateral splanchnic nerve section undertaken on June 6, 1940, and July 23, 1940. She became pregnant one and one-half years later but the pressure remained normal until the last month, at which time it rose to 170/120. She gained thirty-five pounds during the pregnancy but no albumin was recorded in the urine. However, when discharged from the obstetrical service on the twelfth day, blood pressure was 130/96. Four years after the sympathectomies and two and one-half years after delivery, blood pressure was 150/90 in all three positions. It was thought that denervation of the second and third lumbar segments might help and therefore additional lumbar sympathectomies were done with the result that pressures are normal at the time this paper was written. She went to work as a truck driver, and seemed completely adjusted and content.

In this case there seemed to be several factors operating: the rheumatic, the psychologic, and the pregnancy factor. It is open to question whether she

should have been allowed to become pregnant. The additional load seemed to have initiated the recurrence of the hypertension for which additional sympathetic denervations were done. In our opinion she should never become pregnant again.

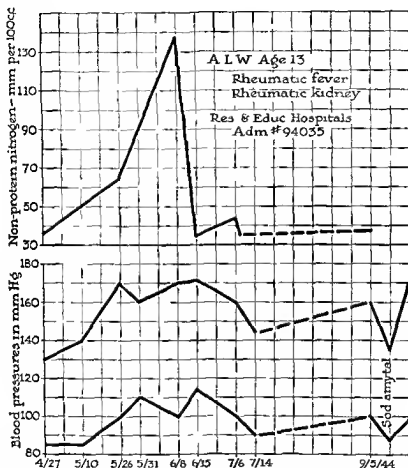


Fig 3.—Nitrogenous retention and rise in blood pressure during an exacerbation of rheumatic fever in the case of A. L. W. a 13-year-old boy. Note the sharp rise in nitrogenous retention, which subsided, however, the rise in blood pressure persists to date without any urinary findings.

CASE 19.—A. L. W., a 13-year-old boy, was admitted to the Research and Educational Hospitals on April 27, 1944, complaining of general weakness and migrating joint pains. He was well until Christmas, 1943, when he developed a sore throat. One month before admission he had another sore throat, after which he became progressively listless, fatigued, and weak. A week prior to admission he had a severe pain in the right ankle; a day or two later the right knee and hip became involved. None of these pains were accompanied by erythema or swelling. There was also dyspnea on exertion for the previous two months.

Entrance.—The temperature was 100° F, pulse 130, respirations 28. Blood pressure was 130/80. Urine was negative for any abnormal elements on May 11 and 24, June 10 and 12, July 1 and 5. Lungs were clear; the pulmonary first sound was heard at the anterior

axillary line in the fourth interspace. There was a split first mitral sound, and a systolic murmur at the aortic area appeared to replace the first sound. The sedimentation rate was 28 mm. on entrance, 17 mm. on May 4, 9 mm. on May 24, and 24 mm. on June 16, 1944. Blood count showed a moderate anemia and a 4 per cent eosinophilia. On May 20 the standard urea clearance was 6 c.c., on May 24 a maximum urea clearance of 12 c.c., on June 8 a standard clearance was 224 c.c. per 100 c.c. of blood. The nonprotein nitrogen on April 28 was 36; it gradually rose to 137 on June 7 and dropped again to 35 on July 8. The urea nitrogen ran a parallel course reaching the peak of 109 on June 7 and dropping to 13 on July 8. This gave the amazing urea ratio of 80 on June 7. On x ray examination the heart showed enlargement to the right and left.

A diagnosis of acute rheumatic fever with mitral and aortic stenosis was made. Most interesting was the rise in blood pressure from the admission figure of 130/80 on April 27 to 140/85 on May 10, 170/100 on May 26, 160/110 on May 31, 170/100 to 156/110 on June 8, 172/110 on June 15, 160/100 on July 6, and 144/90 on July 14. All this occurred simultaneously with the retention of nitrogen and no urinary findings, certainly no red cells to suggest a nephritis (Fig. 3).

On readmission, Sept. 5, 1944, hourly blood pressures varied from 160/110 to 136/83. The latter figure was obtained while asleep under sodium amytal. Urea clearance was 33 c.c. standard clearance. He left with a casual blood pressure (being up and around) of 170/98, there were still no red cells or albumin on repeated examinations, but during the second admission there were hyaline casts. Further study in the outpatient department revealed that the hypertension was limited to the upper extremities, both femorals were only faintly palpable. However, a typical picture of coarctation of the aorta could not be ascertained.

*Comment*—On reviewing this case, it seemed that while at the hospital and during the course of the acute rheumatic fever, a vascular accident occurred, which seriously impaired the renal function and closed his aortic bifurcation. This could have been an embolic or thrombotic process, not unlike the one Scupham and one of us (G de T<sup>13b</sup>) reported in the presence of a diffuse lupus erythematosus.

The significance of this history lies in the fact that under our own eyes there developed a case of juvenile essential hypertension in the course of a rheumatic infection. We have advocated surgery for this lesion.

#### UNCLASSIFIED GROUP

It would obviously be desirable to place all our patients with hypertension in the neurogenic or one of the renal groups. However, in our present state of knowledge this does not always seem possible (Table I).

#### COMMENT

Two groups of workers, Gregory and Levin,<sup>24</sup> and Page and his group,<sup>1</sup> have attempted to use spinal anesthesia with the idea that neurogenic renal vasoconstriction would be abolished, but not the humoral type; if the patient's blood pressure fell markedly a neurogenic type of hypertension was postulated which seemed amenable to sympathectomy whereas the renal, humoral type would maintain the blood pressure and was not fit for surgery. Surgeons using high spinal anesthesia are aware of the fact that blood pressure may often fall to very low level, this being due to a failure of venous return and a poor cir-

culatory adjustment to a sudden demand for compensatory measures.\* In Grimson's animal experiments,<sup>25</sup> low cervical cord section lowered the hypertension of all animals, whether it was produced by elimination of the buffer nerves or after a Goldblatt clamp was applied; this latter, renal hypertension, did not respond as well in such acute experiments, which are not easy to apply to chronic human hypertension. Our observations, on man, dating back many years, have convinced us that in the first place the differentiation of renal from neurogenic hypertension is often impossible, and that the neurogenic phase may well be followed by a renal arteriosclerosis just as repeated attacks of vascular spasm in the digits will result in digital vascular occlusion in Raynaud's phenomena. Conversely, pressor substances originating from the kidney may sensitize the sympathetic-adrenal mechanism as would appear from Heinbecker's experiments.<sup>26</sup> Contrary to expectation, our best results have been obtained in patients in whom renal vascular damage was obvious, whereas the "neurogenic" or "neuroendocrine" type responded poorly. It should be stressed that nervous stimulation not only activates the adrenals and the peripheral vascular bed, but may also affect the hypothalamic pituitary mechanism. In this latter variety, which according to Griffith and co-workers<sup>27</sup> comprises about 5 per cent of all hypertensives, splanchnic nerve section is ineffective. The nervous stimulus mobilizes the posterior pituitary principle, vasopressin, which is identical with the antidiuretic hormone thus acting directly on both the kidney and the peripheral vascular bed.

What is badly needed is a simple clinical test to detect this principle in the blood and so separate this group of patients from the essential hypertensives. They could have pituitary radiation but surgically only section of the pituitary stalk could be effective. In one such human case, the blood pressure actually fell to normal and diabetes insipidus did not develop.<sup>27</sup> We certainly are not advocating this method except to indicate the futility of splanchnicectomy in such a case.

In another paper<sup>2</sup> it was stated that the juvenile patient with hypertension whose basal diastolic blood pressure (after rest, sleep, or sedatives) still exceeds 90 mm. of mercury is the ideal surgical case, that in a second group irreversible changes exist but symptomatic relief is obtained and progress toward a malignant phase may be averted; that the patient in a premalignant or malignant phase has not derived any benefit from splanchnic nerve section in our hands. The conclusions which the present series of observations justify are that the so-called neurogenic group has not responded too well to this operation, whereas the "renal" group, provided renal damage is not too advanced, has responded favorably. Patients with pyelonephritis, post toxic hypertension, streptococcus nephritis, and rheumatic renovascular damage are favorable candidates when the original process has subsided and the resulting renal arteriolar sclerosis remains. There is a possibility that the so-called neurogenic hypertension

\*In their latest experiments, Gregory and his associates (*Arch. Int. Med.* 77: 385, 1946) found that when spinal anesthesia lowered the blood pressure of hypertensives to normal inulin and diodrast clearances fell, this is one more argument in our opinion (but not in the authors') that hypotension induced by spinal anesthesia is not the equivalent of the reduction of pressure following splanchnic nerve section.

while activated by the central nervous system is a pluriglandular type of hypertension governed by the pituitary. Such patients may not respond to splanchnic nerve section and a simple, clear-cut biologic test would be most welcome to separate them from the operable cases.

## SUMMARY

A group of case histories is presented of hypertensive patients who have done well, moderately well, and poorly after splanchnic nerve section. The operation used was a transdiaphragmatic approach and technically left nothing to be desired. The clinical history and renal biopsies have allowed us to separate a group of patients who suffered organic renal damage and showed good response to surgery. On the other hand, the so-called neurogenic group failed to respond even though there was little or no detectable damage. The suggestion is made that such hypertension exhibits a hypothalamic-pituitary stimulation which is not mediated by the sympathetic nervous system.

We are deeply indebted to our medical colleagues at the University of Illinois College of Medicine and St. Luke's Hospital for their cooperative study of the reported cases.

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## FASCIA LATA REGENERATION

### ANIMAL EXPERIMENTATION

J. C. FOSHEE, M.D., GRAND RAPIDS, MICH.

SINCE I had done explorations on the thigh of man for the purpose of observing the process of fascia lata repair in ten patients from whom I had removed fascia lata for various surgical reconstructive procedures,<sup>1</sup> it was now my desire to know certain facts pertaining to this regeneration, which could perhaps never be known except by animal experimentation. I desired to know why the regenerated fascia lata in man consisted of only two layers, whereas the original had three layers. It was my opinion that observation and biopsy of regeneration defects at various lengths of time from several days to a few weeks after it had been made would undoubtedly be of great value in determining this factor. Not only did I desire to determine the rate at which regenerated fascia formed, but also from whence it came, and how it developed.

This investigation began in October, 1944, and was completed in the summer of 1945. Twenty-two operative experiments were performed on three dogs at twelve different times. When two extremities were opened on one dog, as was the case occasionally at one setting, it was considered two experiments. In the few instances in which this was done, a different type of investigation and observation was carried out on each thigh.

At no time was the life of any dog endangered. In fact, not one dog was really ill during the nine months of this investigation. Preoperative sedation with morphine sulfate hypodermically, followed by open drop ether, was the routine anesthesia employed. There were no infected wounds. In two instances a hematoma developed beneath the skin flap which interfered with the desired observation. In each of these two instances the experiment was considered a loss. These two hematomas should not be a surprise when one considers the great redundancy of skin and superficial fascia present in the thigh of the dog. Besides, one cannot apply a pressure bandage to the thigh of a dog as one can in man. Fine silk sutures were used throughout in this work. Each dog weighed approximately thirty pounds. The operative field was prepared by clipping the hair of the thigh, and then shaving it clean. The skin was washed with soap and water, dried, and painted with 50 per cent tincture of iodine. Sterile technique was used in each operative procedure throughout. All wounds were closed with interrupted silk sutures taking the skin, subcutaneous fat, and superficial fascia in one layer.

### EXPERIMENTS

EXPERIMENT 1—Dog 2078, Oct. 11, 1944. The left thigh was opened down to the fascia lata by a vertical incision on the external surface at the junction of the middle and lower third. The fascia lata was cleaned off by pushing the

superficial fat and fascia aside, and a piece of the fascia lata 2 cm. square was removed. Two small vessels were tied with fine silk for hemostasis, and the wound was closed in the usual way. Microscopic study of this specimen showed it to contain three layers identical to that of man, namely, an inner and outer transverse layer, and a middle longitudinal layer (Fig 1).



Fig 1—Normal fascia lata, three layers

**EXPERIMENT 2—Dog 2078, Dec. 6, 1944** The left thigh was reopened by excising the old skin scar to expose the defect made by the previous operation. The reparative process was so extensive and the superficial fascia so dense that it was impossible to ascertain the exact area from which fascia lata had been removed. After that the border of all defects from which fascia lata was removed was marked with fine black silk in order that they might be identified easily when explored again. A specimen was removed which was thought to include the regenerated fascia with a narrow rim of the normal surrounding fascia lata on all sides, but a microscopic study made of slides taken from this tissue proved inconclusive. However, the defect now was greater than ever, and offered hope for a future exploration with a more satisfactory histologic study of the regenerative material. Therefore, the margins were marked with fine black silk interrupted stitches to make identification easy at a subsequent exploration.

**EXPERIMENT 3—Dog 2078, Jan 31, 1945** The left thigh was reopened by excising the old scar and dissecting the flaps on either side. For the first time two layers of superficial fascia were found in a dog, each of which had under-

gone hypertrophy from operative trauma. In this case both layers were cleanly dissected off the true fascia lata until the defect made by the previous operation and outlined by the black silk came into view plainly. There was a layer of grayish-white fascial membrane growing toward the center of the defect from the fascia lata margins on all sides. The membrane seemed to come from the normal fascia lata, and was in continuity with it. There was an area about 1 cm. in diameter in the middle of this defect which had not yet been filled in by this membrane of new fascia. This new membrane seemed of a lighter gray, more of the color of normal fascia lata toward the periphery of the defect, and darker in color toward the center. An incision was made through the normal fascia lata all the way around the defect about 1 cm. from the edge, and a block



Fig. 2.—Regenerated fascia lata tapering off. Outer layer becomes thinner, inner layer stops in the lower right. Few muscle bundles in the lower left.

of tissue including this rim of normal fascia lata and the new regenerated fascia was dissected up from the muscle below. The edges of the normal fascia lata were a little more adherent to the muscle than normally, but the new regenerated fascia growing across the defect was not, and the new fascia became progressively thinner as it grew toward the center of the defect (Fig. 2). The margins of this defect, now larger than before, were marked by frequent interrupted stitches of fine black silk, and the skin and subcutaneous tissues were closed in the usual way.

EXPERIMENT 4—Dog 2078, Jan. 31, 1945 The right thigh was opened for the first time. The fascia lata was exposed and a portion of fascia lata 3 cm. square from the lowest and strongest portion near the knee was removed. The

border of the defect was marked with continuous stitch of black silk, and the wound was closed in one layer of interrupted silk in the usual way

**EXPERIMENT 5.**—Dog 2078, Feb. 21, 1945 The left thigh was again opened by excising the previous skin scar. Superficial fascia and subcutaneous tissues were dissected away to either side with moist gauze and scissors until the defect and its reparative process came into plain view. The regenerated fascia of the entire defect with 1 cm. of normal fascia lata all around the marked black silk was removed for study. The specimen grossly gave the impression that the regenerated fascia was coming from the margins of normal fascia lata on all sides. Toward the center it was of a grayish-red color, smooth, and tapered off, getting thinner at its inner edge near the center, and there was an area in the center  $1\frac{1}{2}$  cm. in diameter that was void of this membrane. The fibers of the red muscle showed very plainly in the center for they were not covered by the regenerated fascia. In Fig 3 is shown, on the left half of the slide, the edge



FIG 2.—Normal fascia lata with silk markers in left; regenerated fascia lata with only inner and outer layers continuing

of two black silk markers in the margin of normal fascia lata containing three layers; whereas, in about the center of this view the middle layer terminated and the hypertrophied inner and outer layers fused to continue as one layer of regenerated fascia lata. According to Weller, the area in the left half in front of the silk and between the inner and outer layers proximal to their union was proliferating connective tissue looking more like regenerated fascia than ordinary scar tissue. This was undoubtedly a proliferation of the middle layer where the silk and trauma had partly destroyed it at its very margin.

**EXPERIMENT 6.**—Dog 2078, Feb. 21, 1945. The right thigh was reopened. The defect, which had been outlined with fine black silk sutures in the very lowest part of the fascia lata, was excised taking a very narrow margin of the normal fascia lata on all sides (Fig 4). This left a rectangular defect about 3 cm. long with the long axis of the thigh and  $3\frac{1}{2}$  cm. wide transversely with the thigh. The fascia lata above this region was now freed of its overlying superficial fascia and subcutaneous fat for a good distance; another piece of fascia lata of identical size and shape was removed above the first defect, but leaving an undisturbed piece of fascia lata between the two defects  $1\frac{1}{2}$  cm. wide with the long axis of the thigh and  $3\frac{1}{2}$  cm. long transversely with the thigh. In other words, there was an intervening bridge of normal fascia lata across the lower third of the thigh, undisturbed, between the two defects. The edges of this



Fig 4.—Left half normal fascia lata margin; right half, regenerated fascia lata. Note middle layer terminates at point X, even with the black silk marker.

normal strip of intervening fascia lata were marked with a continuous suture of fine black silk. It was obvious that this would be of great help in the study of the regenerated fascia that should develop in these two defects since its direct relationship grossly and microscopically to the intervening strip of normal fascia lata could be accurately observed.

**EXPERIMENT 7.**—Dog 2078, April 11, 1945. The right thigh was reopened. The two defects and intervening strip of normal fascia lata, with its fine black silk thread clearly outlining its borders, was very vivid after the superficial fascia and fat had been cleanly dissected away. The two defects were filled in with a new layer of smooth fascia which was of the same color and apparent thickness as that of the normal fascia lata strip in between, as well as the normal

fascia lata all around. Both defects and all surrounding normal fascia lata were covered with one common thin external sheath. The whole would give one the impression that no fascia lata had ever been removed. But on palpation it could be felt that the intervening strip was probably just a little thicker. However, without the fine black silk markers it would have been impossible to distinguish the intervening strip of fascia lata from the regenerated fascia lata on each side.

The normal fascia lata was cut transversely across the thigh  $2\frac{1}{2}$  cm. proximal to the transverse normal strip and  $2\frac{1}{2}$  cm. distally. These transverse incisions extended into the normal fascia lata margins mesially and laterally for 1 cm., and their two ends were connected by two longitudinal incisions through the normal fascia lata margins 1 cm. from their edges. This block of tissue consisted of the regenerated fascia of the two previous defects and the intervening normal fascia as well as 1 cm. of fascia of the mesial and lateral margins enclosed in common internal and external sheaths. The slides (Fig 5) show that the strong middle layer of longitudinal fibers do not regenerate nor extend themselves at all, but remain static at the silk thread markers on either side of the intervening strip of normal fascia lata, whereas the inner and outer layers of transverse fibers cut somewhat obliquely with their course do extend onward directly by continuity across the defect together as one dense layer of well-organized parallel fibers of fascia, and each layer undergoes hypertrophy to compensate in thickness and strength required in the absence of the middle layer.

EXPERIMENT 8—Dog 2077, Oct 11, 1944. An incision was made over the lower anterolateral surface of the lower third of the left thigh. The fascia lata was exposed and a piece  $2\frac{1}{2}$  cm. square was taken up, turned one quarter around, turned over so that the outer surface became the inner surface, and resutured in position with fine black silk. The skin was closed in the usual way.

EXPERIMENT 9—Dog 2077, Jan 17, 1945. The block of fascia sutured down with silk in Experiment 8 together with 1 cm. of the normal fascia around it was removed. The replaced block was exactly the same thickness as that of the surrounding fascia, and the inner and outer sheaths were in continuity. Only by the fine knots of black silk could the area be outlined. The specimen (Fig 6) was cut transversely to the long axis of the middle longitudinal fibers on the margin as seen in the left one-third of the specimen, and parallel to the middle longitudinal fibers in the block that was turned one quarter around as noted in the distal two-thirds of the slide. The line of union between the block and the margin may be seen directly between the two silk sutures. The middle longitudinal layer was thicker to the left of this line of union than to the right, and the inner and outer transverse layers were thicker and better developed to the right than to the left of the silk threads and this line of union. This did not show as distinctly in this one field as it did when studied under the microscope with a view of a larger area, in which it was very obvious. This confirms the work of Kleinschmidt.<sup>2</sup> That is, when the longitudinal fibers were

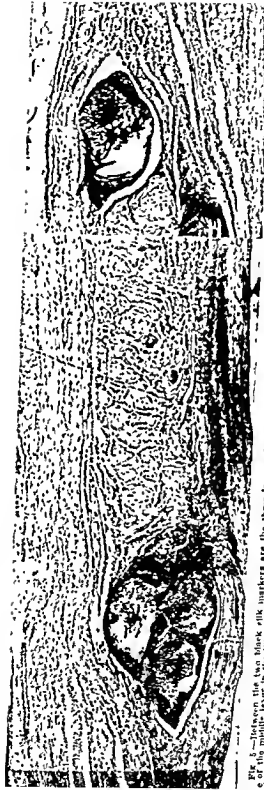


Fig. 5.—Between the two black silk markers are the three layers of the intervening strip of normal fascia lata. On each side, right and left, there is a total of the middle-layer in the two areas of regenerated fascia lata. But the inner and outer layers have extended across both defects in continuity from their respective layers of the normal fascia lata.

placed so that they did not take up the pull that was usually required of them they became thinner; whereas, the inner and outer transverse layers became thicker and better developed from taking on the pull which the middle longitudinal fibers previously maintained. Some of the inner and outer layers of transverse fibers were outside of the silk suture on either side, whereas all the middle longitudinal fibers were seen plainly in the middle with a good amount of the inner and outer transverse fibers running between the middle fibers and the silk sutures.



Fig 8.—Flattened and atrophied middle layer of bundles to the right of silk with hypertrophy of the inner and outer layers

**EXPERIMENT 10**—Dog 2077, Jan 31, 1945 The left thigh was reopened by making an incision around the old scar and taking a block of elliptically shaped tissue down through the fascia lata. A study of the tissue revealed the identical layers found in the normal thigh; the skin, subcutaneous fat, two layers of superficial fascia, a thin layer of adipose or areolar tissue and the fascia lata. The fascia lata defect with its regenerated fascia was in the bottom of this block. A study of this defect made by removal of the block of fascia lata in Experiment 9 showed that it had half filled in with a new, thin, slightly reddish layer of fascia lata extending from the margins, and it was covered with a thin sheath which was in continuity with the sheath of surrounding fascia lata. The muscle fibers beneath were faintly visible because of the thinness of the new regenerated fascia which was somewhat transparent. The center of this defect for an area of 2 cm. square was not filled in with regenerated fascia and the muscle was bare. This regenerated material was removed along one side with silk sutures, which were placed two weeks before for identification,



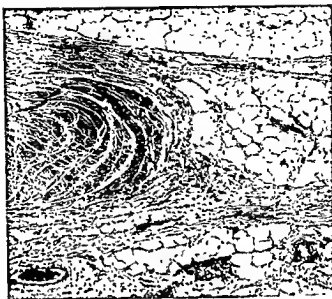


Fig 7—Three layers of normal fascia lata of left third. Two layers of regenerated fascia lata in right two-thirds. Common external sheath above

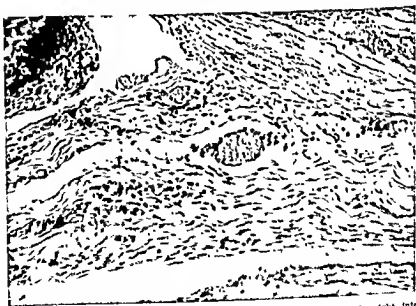


Fig 8—Left upper corner, black silk marker on margin of defect. To the right, internal and external layers fuse and continue on in orderly fashion to form the regenerated fascia lata. Common internal sheath below.

together with a little of the margin of normal fascia lata. A slide (Fig. 7) made from this tissue shows the margin with the three usual layers in the left third of the slide and the new regenerated fascia just forming, fourteen days old, occupying the right two-thirds. It is interesting to note that the internal layer was extending on independently of the external layer from which it was separated by adipose tissue, and it was fully twice as thick and as well developed as the external layer. Some of the fibers of the internal and external layers have united just in front of the termination of the middle layer.

EXPERIMENT 11—Dog 2077, Feb. 21, 1945. Again the left thigh was reopened to observe the defect made three weeks before, and it was found that the regenerated fascia lata had spread almost all over the thigh defect. There was an area 1 cm. wide in the middle which was not covered with the regenerated fascia. The muscle fibers here were bare. The regenerated fascia defect and a little of the normal fascia lata margin was removed. A slide made from the margin is shown in Fig. 8. Before the incision in the leg was closed the margins of this very large defect which was about four inches square were marked with continuous black silk suture for further identity.

EXPERIMENT 12—Dog 2077, April 11, 1945. Following this experiment a large hematoma developed in the wound, which was evacuated. An interrupted suture or two was removed in the middle of the wound. After some clots were expressed the wound healed quite readily, but it was feared that any future value from opening the thigh would be lost. However, to make certain, the thigh was opened and it was found that superficial fascia proliferation and edema so obscured the field that the experiment had to be considered a loss. The wound was closed by primary suture and a temporary pressure bandage applied.

EXPERIMENT 13—Dog 2077, April 11, 1945. The right thigh was opened for the first time and Experiment 7 of Dog 2078 was repeated. A wide area of the fascia lata was freed of its superficial fat. Two blocks of tissue 3 cm. square were removed, leaving an intervening piece of undisturbed fascia lata between the two defects  $1\frac{1}{2}$  cm. wide. The two edges of the intervening piece of normal fascia lata were marked with a very fine continuous black silk suture, and the skin was closed.

EXPERIMENT 14.—Dog 2077, May 9, 1945. The right thigh was reopened by an elliptical incision around the old scar. After the skin and subcutaneous fat had been incised and brushed aside with moist gauze, a well-defined layer of superficial fascia came into view. It was dissected off and then another layer of superficial fascia appeared which was thicker than the first. It was dissected off. With moist gauze, a little fat and areolar tissue were brushed away to expose the regenerated fascia lata immediately beneath with the intervening strip of normal fascia lata well outlined with the black silk suture. Grossly the appearance of the normal fascia lata between, at each end, and at the sides of the defects seemed of the same thickness, color, and consistency as the regenerated fascia of the defects. Were it not for the black silk sutures it would have been

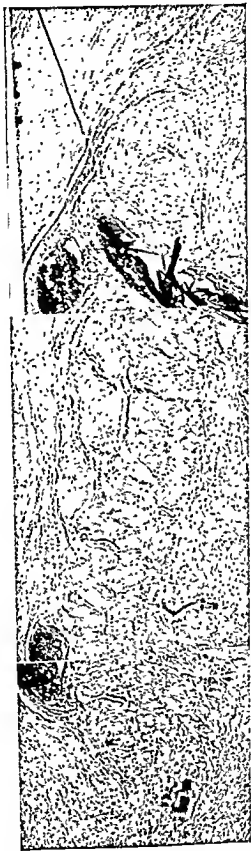


Fig. 9—In placing the silk a drop hit so that the termination of the middle layer which is the very margin of the normal fascia lata is just outside the black silk sutures. The inner and outer layers, only, continue onward to the right and left to form regenerated fascia lata.

impossible to identify the defect. The external sheath of the normal fascia lata continued over the defect and was in direct continuity without any scar tissue or contracture whatsoever. The regenerated fascia lata of the defects and the intervening normal fascia lata strip were removed en masse. When they were stripped away from the underlying muscles, it was striking to note the fact that they all appeared as one single piece of fascia covered by a common internal and a common external sheath, which extended across from the normal fascia lata. No one part of the block was any more adherent to the underlying muscles than the other. In fact, it was all in loose approximation as was the normal fascia lata elsewhere. Several blocks of tissue were taken in this specimen for histologic study. The most interesting block perhaps is the one taken through the middle of the intervening strip of normal fascia lata and extending on into each defect to the right and to the left, each for 1 cm (Fig. 9). Under high magnification the silk sutures appeared to be a little inside the outer edge of the middle longitudinal fibers. Of course, this was a continuous stitch and it was placed a little inside in order that it would be secure. But it showed very definitely that the well-outlined middle longitudinal layer shown in bundles had not regenerated either to the right or to the left, but the inner and outer transverso layers have extended onward in direct continuity without a waver or hesitation to form the regenerated fascia lata, their formation when the whole slide was studied in many different fields showed that their thickness had compensated for the absence of the middle layer in maintaining the strength and function of the normal fascia lata. This accounts for there being no depression or thinning out of the fascia at the site of the defects as shown by gross and microscopic examination. The same thing was true in Experiment 7. In other words, the inner and outer layers seem actually to be hypertrophied as they cross the defects.

EXPERIMENT 15—Dog 2079, Oct. 11, 1944. The left thigh was opened to expose the fascia lata in the lower third of the outer surface. A piece of fascia lata 2 cm. square was removed, turned one quarter around, but not turned over, and sutured into place with interrupted fine black silk. Above this area another small piece of fascia lata was taken for a study of the normal fascia lata of this dog (Fig. 10), and it shows the normal three layers of fascia lata.

EXPERIMENT 16—Dog 2079, Jan. 17, 1945. A block of fascia lata containing the block sutured into place with the margin of the normal undisturbed fascia lata on the four sides was removed en bloc, containing the fine silk knots which identified the quarter-turned block of fascia. The edges of this larger defect were marked with fine black silk sutures for future identity. A section made for study through the margin of the normal undisturbed fascia lata and the graft (Fig. 11) shows in the left fourth the middle longitudinal layer, cut obliquely and nearly parallel to its fibers, to be thicker and stronger than either of the outer layers as would be expected in the undisturbed margin. Whereas in the right half, which is the graft turned quarter around, the middle layer which is now a transverse layer was not as dense as the hypertrophied internal

layer, and about as dense as the outer layer. The inner and outer layers have taken on the pull formerly performed by the middle layer. X to Y is the line of union of the graft and the undisturbed fascia lata margin. This further verifies the findings of Kleinschmidt<sup>2</sup> and Experiment 9 of this article.

EXPERIMENT 17.—Dog 2079, Feb 21, 1945. The left leg was reopened to inspect this large defect and a beautiful specimen was observed showing the normal margins of fascia lata marked out with interrupted black silk previously placed, and a new fascia lata one-half as thick as the normal going completely across the defect. The external sheath of the normal fascia lata was in continuity cross the new fascia lata. In the left two-thirds can be noticed the three layers of normal fascia lata with the middle layer terminating, and in the outer third the inner and outer layers of transverse fibers, only, continue on to form the new thin regenerated fascia (Fig. 12). The defect was again marked with silk and the skin closed.

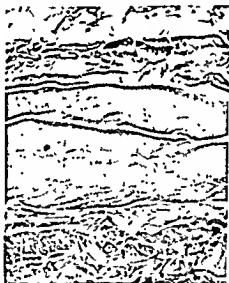


Fig. 10.—Normal fascia lata, three layers.

EXPERIMENT 18—Dog 2079, Feb 21, 1945. The right thigh was opened for the first time and a piece of fascia lata 4 cm. square was removed. The edges of the defect were marked with an interrupted layer of fine black silk. High magnification of this area (Fig. 13) shows the three layers in normal fascia lata.

EXPERIMENT 19—Dog 2079, March 9, 1945. The left leg was reopened, and the large defect heretofore outlined with fine black silk was inspected. It was contracted a bit, being only about two-thirds the size expected, and it was filled in with a thin layer of regenerated fascia lata. In the center it was so thin

that the muscle beneath could be visualized, but on its periphery it was too well formed for that, and the whole was covered with a sheath from the normal fascia lata which came across in continuity. A section (Fig 14) shows a picture similar to that shown in Experiment 17. The middle layer terminated in the left third and the inner and outer layers extended across to form the new fascia.

EXPERIMENT 20.—Dog 2079, March 9, 1945 The right thigh was reopened, the defect observed, and in this instance the superficial fascia had dipped down



Fig 11 — Left third is normal margin with thick middle layer and thinner inner and outer layers Right half is the graft with the thicker inner and outer layers and thinner middle layer



Fig 12—Left two-thirds shows three layers of normal fascia lata. Right one-third shows two layers of regenerated fascia lata.



Fig 13—Strong middle longitudinal layers cut transversely. Inner and outer transverse layers cut parallel or somewhat obliquely.



Fig 14—Three layers of normal fascia lata in left third with inner and outer layers extending across in continuity



Fig 15—Confusion of various layers.



into the defect to form scar tissue, the first that had been observed. It was rather difficult to dissect the superficial fascia off the defect. The superficial fascia had undergone so much hypertrophy and hyperplasia that it was as thick as one would expect fascia lata to be, but not as well outlined. After it was finally dissected away, the normal fascia layer with the black silk below was visible, but the defect had contracted and a large block was removed containing the silk in the hope that a section running from the margin of the normal fascia lata to the regenerated material in the defect might be found. The defect was again marked with fine black silk sutures. Microscopic study of this section (Fig. 15) shows a confusion of the various layers. At the top can be noted the sheath and a few parallel fibers of the external layer which ran across to the right and left of the black silk in continuity. Immediately beneath were some bundles of the middle layer to the right of the silk, and from there on downward below the level of the silk there was a mixture of layers, and marked hypertrophy of the inner layer. In the left lower center there were a few transverse fibers which were surrounded by fibers of the internal layer. In the right lower corner was the thickened sheath of the internal layer. This was an irregular pattern, and the only one so far observed.

**EXPERIMENT 21.**—Dog 2079, April 11, 1945. Thirty-three days later the right leg was reopened. Both layers of the superficial fascia were dissected off, each separately. The deeper layer was attached to the fascia lata with long trabeculations through an intervening layer of areolar tissue. When that was brushed away with a moist sponge the silk pattern, which outlined the defect, was found in the fascia lata below. A specimen 5 cm. square including normal fascia lata in the left half and the regenerated fascia in the right was taken for study. The silk stitches were in the middle of this specimen. A continuous silk suture was placed around the margin of the defect for future identification. A section was taken at the junction of the normal and the regenerated fascia lata. Microscopic study of a slide from this area (Fig. 16) shows the three layers of the normal fascia lata to the left of the silk and only two layers to the right, namely, the inner and outer layers which had extended across in continuity. The middle layer had not regenerated and stopped abruptly at the site of the silk marker.

**EXPERIMENT 22.**—Dog 2079, June 9, 1945. The wound was reopened and a suture of black silk was observed around the previous defect. A new layer of regenerated fascia lata extended across the defect. Microscopic study of a slide made from this area shows the termination of the middle longitudinal layer to the left and at the site of the black silk (Fig. 17); whereas, the inner and outer layers continue on and merge into one to form the thick regenerated fascia lata across the defect. The well-organized internal layer of parallel fibers which was more dense than the external layer extended across in continuity to make a thick substantial layer. Both layers combined made a firm layer of regenerated fascia lata enclosed within a common external sheath shown at the very top and a common internal sheath, which was not shown in this field.

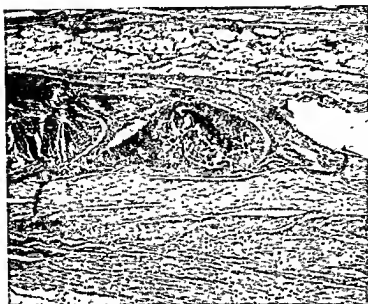


Fig 16.—Middle layer stops left of silk inner and outer layers continue on.

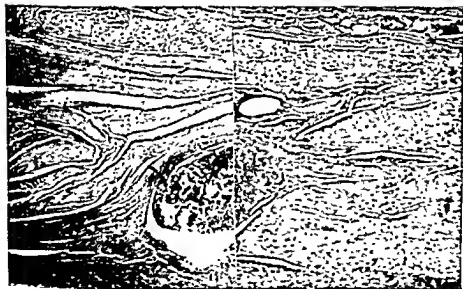


Fig 17.—Three layers at the left of silk, two layers, inner and outer, continue on to the right of silk.

## COMMENTS

The use of living fascia lata in reconstructive surgery is continually becoming of greater interest and importance. For many years large fascia lata grafts have been used in arthroplasty of the large joints. Not long ago Singleton and Stehouwer<sup>3</sup> reported the use of large fascia lata grafts in the repair of inguinal hernias. More recently Wangenstein<sup>4</sup> has used practically all the fascia lata as a pedicle flap to fill in the defect in the repair of large abdominal incisional hernias. No effort was made by the authors, or anyone I know, to attempt to reconstruct a fascial covering for the muscles of the thigh from which these large fascia grafts were removed. Such a repair would be impossible anyway. It is important to know what happens to a defect produced in fascia lata.

## CONCLUSIONS

1. Twenty-two experiments on the fascia lata of dogs are reported. Regenerated fascia lata has been studied at various phases and stages from the fourteenth to the ninety-seventh day of its formation.

2. The inner and outer transverse layers regenerate by extension directly from their respective layers of the adjacent normal fascia lata together with their sheaths and blood vessels. The middle longitudinal layer does not regenerate.

3. In a medium-sized defect the average rate of regeneration is as follows: At the end of two weeks the regenerated fascia lata is only a thin veil. It becomes more dense rapidly. At three weeks it is a well-defined membrane. At one month it is half as thick as normal fascia lata, and at two months it is grossly and microscopically as thick as normal fascia lata. In a very large defect the process of regeneration may be slower, but in a smaller defect it may be so rapid that the regenerated fascia lata in one month will become as thick as the normal fascia lata.

4. Since the middle layer is always absent in the regenerated fascia lata, the inner and outer layers undergo hypertrophy and hyperplasia to compensate for the absence of the middle layer.

The author wishes to express his sincere appreciation to Dr. Frederick A. Collier, Chairman and Professor of the Department of Surgery of the University of Michigan at Ann Arbor, for the use of the laboratory of Experimental Surgery of the University and all of its facilities, and to Dr. C. V. Weller, Chairman and Professor of the Department of Pathology of the University for the histologic studies which he made in this research, and to Mr. W. J. Troy, Attendant in charge of the Experimental Laboratory, profound gratitude is expressed for his able assistance in that he administered the anesthesia in every experiment and cared for the animals nine months without an accident.

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## FASCIA LATA REGENERATION

### FINAL REPORT

J. C. FOSHEE, M.D., GRAND RAPIDS, MICH.

(From the Department of Surgery, Butterworth Hospital)

THERE is a certain curiosity and inquisitive attitude in one's mind toward the reparative processes that take place when a structure so large and so important as fascia lata is removed in part or in whole. In my preliminary report upon the subject two years ago<sup>1</sup> I presented the first evidence that has appeared in the literature that fascia lata when removed from man does regenerate completely enough to be used again in surgical procedure should the demand for its use so arise. At that time five cases of regeneration were reported which I had personally observed. Since that publication, observations have been made by other surgeons in one or more cases that similar regeneration occurred, but no histologic studies were made. Coller<sup>2</sup> observed regeneration of fascia lata following a Kondoleon operation for elephantiasis of the lower extremity including the thigh in which the fascia lata had been removed in its entirety. The patient returned with a recurrence of elephantiasis and was re-operated upon. A large piece of new substantial fascia was removed from the thigh at the second operation, which looked like fascia lata to Coller, and he mentioned my work at that time to his associate who performed the operation. But, unfortunately, that specimen of fascia was lost at the University Hospital so that I was unable to obtain a specimen of it for study.

Such regeneration has also been observed by Smith<sup>3</sup> in a case in which he reopened a thigh to obtain more fascia lata in a procedure of plastic surgery. Singleton and Stehouwer<sup>4</sup> stated that they had observed the regeneration of fascia lata, but that they did not make biopsy or histologic studies of the regenerated material. They took it to be scar tissue. It is unfortunate that none of these surgeons made a histologic study of the regenerated fascia for, as I have shown and will show, it is not scar tissue but quite to the contrary it is a structure of well-organized layers of certain parts of the normal fascia lata, such layers having their own sheaths and these sheaths combined in a common sheath, each sheath with its own minute blood vessels as Kleinschmidt<sup>5</sup> and I have heretofore shown.

When opening the thigh in an occasional case in which the subcutaneous fat and superficial fascia does not peel off the regenerated fascia so readily, one might form the opinion that he is dealing with a layer of scar tissue. I have observed one such case, but this is by far the exception rather than the rule, and when in such a case the regenerated fascia is dissected off the underlying muscles it becomes very evident that one is dealing with a real sheath of substantial fascia that is loosely attached to the muscles by thin trabeculations exactly as is normal fascia lata. When this layer of material is subjected to

careful histologic studies, it will show definite regenerated layers of fascia lata always following a certain pattern as I have found repeatedly and reported previously.

In my preliminary report it was shown that normal fascia lata is comprised of three layers, namely, an inner transverse layer, an outer transverse layer, and a stronger middle longitudinal layer; that each layer is enclosed in its own fine sheath; and all three layers are enclosed in a denser common sheath. Certain proofs were presented that it was the inner and outer transverse layers that regenerated.

As further proof, five additional personal cases of regenerated fascia lata have been studied. Knowledge has been gathered from these cases which, it is hoped, will show conclusively the exact nature of the regeneration and other facts of value concerning the new fascia which forms.



Fig 1A.—Normal fascia lata with outer transverse layer, middle longitudinal layer, and inner transverse layer. Each layer enclosed in a thin delicate sheath.

#### CASE REPORTS

**CASE 1.**—Mrs. P., aged 51 years, upon whom was performed an abdominal total pan hysterectomy, May, 1938, for carcinoma of the fundus of the uterus, and whose immediate recovery was uneventful, returned two years later with an incisional hernia. At the time of operation she was quite obese and the obesity had increased markedly. She was a school teacher, who could ill afford to have the hernia repaired except during the summer vacation. During the following summer when she needed further recuperation, and there was uncer-

tainty of the ultimate success of the irradiation of all the cancer, operation was discouraged, but in the summer of 1942 when she was apparently enjoying good health she insisted that the hernia, which was becoming larger and more troublesome all the time, be cured by surgical repair. Since it has for many years been my custom to repair nearly all ventral and incisional hernias with fascia lata, on July 23, 1942, the hernia was repaired, using among other material for suturing two pieces of fascia lata each one-half inch wide, and seven inches long, taken from the right thigh. About one year later, June 29, 1943, she permitted reopening of the right thigh to inspect the process of regeneration. It was found that the old fascia margins had spread apart for a distance of two inches and the area between had filled in with a smooth layer of fascia not quite as thick as the normal fascia lata margins but of the same color, and not more adherent to the overlying superficial fascia and underlying muscles than was the normal fascia lata. A specimen three inches square in the center was taken, which included the full width of the regenerated fascia lata and one-half inch of the medial and external margins of the old fascia. Grossly the inner and outer layers of regenerated fascia appeared in continuity with the corresponding inner and outer layers of the margins of fascia lata on both borders of the specimen, but the middle longitudinal layer of white fibers was not apparent in the regenerated part. In Fig 14 are shown very clearly the three distinct



Fig. 1B—Three layers of normal fascia lata on the left two layers of regenerated fascia lata on the right

layers in the normal fascia lata margin of the specimen cut a little obliquely instead of exactly transversely as intended. This cannot always be avoided. The inner and outer layers combined were about as thick as the middle layer. In Fig 1B, a little further along in the specimen at another site at the end of the normal fascia margin and the beginning of the regenerated fascia, are shown the playing out and termination of the middle layer of fibers with the inner and outer layers extending across in continuity. They each became more dense as they fused together to form a thick layer of regenerated fascia.

Case 2—Mr. T., aged 52 years, on Oct. 30, 1928, had two strips of fascia lata taken from the right thigh and used for the repair of an incisional hernia in the upper right abdominal wall, which had followed a right paramesial incision for an operation for gastroenterostomy for the cure of a chronic stenosing duodenal ulcer in 1927. On Jan. 22, 1942, this patient submitted to operation for a recurrent direct inguinal hernia operated upon at first three years before, elsewhere. Fascia lata sutures were again removed from the right thigh of the patient for the repair of the hernia. This patient was a very large, obese man,

a heavy beer drinker, who lived an easy life and seldom used the skeletal muscles. In such a case we may expect to find very thin fascia everywhere in the body, hence a thin regenerated fascia. Exactly that was found. The medial margins of the fascia lata defect created by the removal of the fascia strips fifteen years before had retracted to the midline anteriorly and the external margins had retracted four inches laterally and posteriorly. There was just



Fig. 2A.—Very thin outer layer, an inner layer three times as thick and a very dense middle layer.

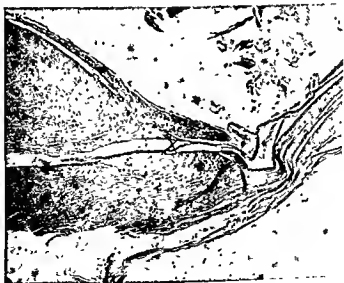


Fig. 2B.—Normal fascia lata margin of left two-thirds; regenerated right one-third.

enough of the old fascia lata left of the external shelf to make three strips three eighths of an inch wide for the repair of this hernia. The intervening wide defect made fifteen years before was filled in with the thinnest of regenerated fascia lata which had been observed so far. A specimen of it was incised, taking a little of the medial border of the old fascia lata attached. In Fig. 2*f* are shown the three layers of the normal fascia border, and in Fig. 2*B* just one field further on in its very center the middle layer of fibers comes to a blunt ending. An attempt was made to cut this specimen transversely with the long axis of the thigh, but it was cut somewhat obliquely. The wide inner transverse layer of fibers goes on into the regenerated material after forming the curl and kink seen in the right half of the field. The outer transverse layer in this case was almost insignificant, being about one fifth as thick as the inner layer and only its sheath and a few of its fibers were seen to continue with the internal layer to form the regenerated fascia to the right. In Fig. 2*C* is shown how the external layer farther in the regenerated fascia has faded out completely. The chief structure of the regenerated fascia was the inner transverse layer of the normal fascia lata. This accounted for this regenerated fascia being thinner than usual.



Fig. 2*C*—Continuation of thin regenerated fascia, inner layer thins out at *X*.

CASE 3.—Mr. S., aged 58 years, came on the surgical service March, 1941, with an acute exacerbation of a chronic intractable ulcerative colitis. He was in a critical condition and became worse every day in spite of all medical measures. After ample preparation an ileostomy was performed. The patient was so well afterward and so content that he refused colectomy although he occasionally had some mild residual recurrent symptoms. On Sept. 5, 1942, it was necessary to operate on him as an emergency for a strangulation of intestine in an incisional hernia below the ileostomy. He was an obese and inactive man. The use of living fascia lata sutures was deemed advisable, and three strips each three eighths inch wide and seven inches long were removed from the right thigh for the repair. A cure of the hernia resulted. On Aug. 23, 1943, or about one year later, he kindly consented to have the thigh reopened for the purpose of studying and taking biopsy of the regenerated fascia lata. He was the only patient that had been seen who had a hernia of the vastus muscle one year after fascia lata had been removed, but it was confined strictly to the upper half of the incision in the thigh. Obviously it would be interesting to discover the reason for this unusual phenomenon. Under local anesthesia the old incision was opened. The superficial structures were carefully dissected off the regenerated fascia that filled the defect. While dissecting up the superficial fascia, fat, and skin in one layer from the regenerated fascia beneath, much to my surprise, the reason for the herniation was revealed. In the lower half of the defect a new well developed regenerated fascia lata had formed, whereas in the upper half the





Fig 4B—Two layers of regenerated fascia lata



Fig 4C—Three layers of fascia lata margin.

CASE 5—Mr. H., aged 63 years, had the most prominent role in all of the studies of the subject. In August, 1941, he submitted to operation for a cure of a right indirect inguinal hernia. Two wide, long pieces of fascia lata were removed from the right thigh for the repair. A third piece of normal fascia lata was removed for histologic study (which was described in Fig 1 in the preliminary report<sup>1</sup> on this subject). On Dec 5, 1943, this patient returned with a large indirect inguinal hernia on the opposite side. Operation for its cure was performed two days later, and again living fascia lata sutures were removed from the right thigh. The old skin scar was excised and the flap of skin, fat, and superficial fascia was carefully dissected back in one layer to expose below all the defect and regenerated fascia lata which had resulted following the previous operation of two years before. The following description was taken from the operative notes:

Remembering that this patient had rather thin normal fascia lata originally, it was thought that the regenerated fascia lata appeared nearly as thick as did the former normal fascia lata. The whole elliptical area was filled in with a layer of regenerated fascia at least three fourths as thick as normal fascia lata and not quite as white. Grossly it did not contain visible longitudinal fibers, whereas they were plainly visible in the margins of the normal fascia lata.

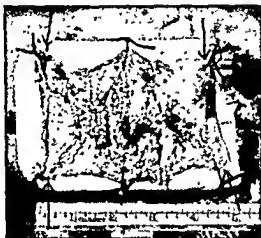


Fig 5A—Arrows point to narrow normal fascia lata margins the wide intervening material is regenerated fascia lata.

An incision was made longitudinally parallel with the long axis of the defect along the mesial edge of the normal fascia lata, taking 1 cm. of that edge for a distance of three and one half inches. A similar incision was made in the external shelf. A transverse incision was made at the ends of these two parallel incisions connecting them and thus freeing a block of regenerated fascia with 1 cm. of normal fascia lata attached to either side, the whole of which was three and one half inches long and four inches wide. This regenerated fascia stripped off the muscle with the same ease as did the normal fascia lata. Grossly it had a visible capsule or sheath on its internal and external surfaces, of a glistening, grayish white color, which was in direct continuity with that of the normal fascia lata on both surfaces. The external surface contained a few tags of fat as did the normal fascia lata. The inner surface had a few fine trabeculae and small blood vessels extending to the muscle as did the normal fascia lata. Two long fascia strips three-eighths inch wide were taken from the remaining part of the lateral shelf of normal fascia lata to repair the hernia. (One of my colleagues, a former naval medical officer in World War I, who is marine minded, saw this specimen and remarked, "Now you have a specimen from shore to shore.")

In Fig. 5A is shown the gross specimen of regenerated fascia lata with a narrow rim of normal fascia lata on each side. The cutting of this specimen was ingenious and it was

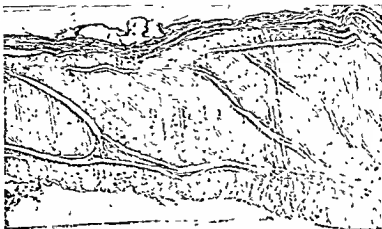


Fig. 3A.—Outer transverse, middle longitudinal, and inner transverse layers

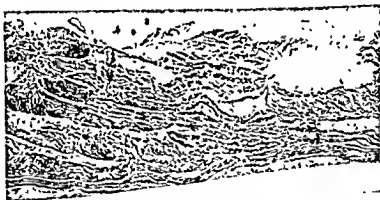


Fig. 3B.—Middle layer stops at X, inner and outer layers continue as the regenerated fascia.

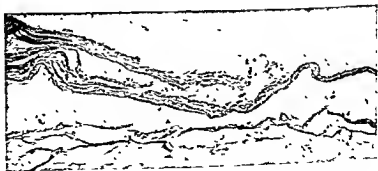


Fig. 3C.—Inner layer stops, outer goes on tapering off.

defect was filled in only by crisscross fibers of fibrous tissue which formed a coarse network structure from one of the old normal fascia margins to the other. In Fig 3A is shown a cross section of a piece of normal fascia lata which was taken for histologic study at the time that the fascia lata sutures were removed for the hernial repair. The weakness of the normal fascia was evident. The outer transverse layer was so thin it was of little use. The inner transverse layer was twice as thick as the outer layer, but less than one third as thick as the middle layer. In Fig. 3B are shown a termination of the middle layer of fibers at the fascia margin (X) and a continuance of the inner and outer layers in their separate sheaths to form the regenerated fascia lata. Soon the one layer (Fig. 3C) stops, but the other layer, the superficial one in this instance, continues onward, tapering more as it goes. This thinning out of the regenerated fascia allowed the bulging of the muscles of the thigh in this defect.

CASE 4.—Mr. A, aged 43 years, was operated upon Feb 23, 1942, for a cure of a bilateral inguinal hernia, direct and indirect, combined. The ordinary Bassini technique was used without the use of fascia lata sutures. On Aug 2, 1942, he was reoperated upon for a recurrence on the left side, and two pieces of fascia lata were used, each one half inch wide



Fig 4A.—Left half is the normal fascia lata, three layers, the right half is regenerated fascia lata, two layers

and six inches long. They were removed from the left thigh. A cure resulted. Eight months later the patient permitted reopening of the thigh to obtain regenerated fascia for study. The old fascia margins had spread apart in the middle for a distance of two inches. The defect was filled in with a good, thick, shiny layer of fascia. The inner and outer layers appeared to be in continuity with the inner and outer layers of the normal fascia lata. A section three inches wide was taken transversely through the center of the regenerated area and it included 1 cm. of the margins of the normal fascia lata on its medial and lateral edges. In Fig 4A are shown, in the left one third, all three layers of the normal fascia lata margins well developed, with a part of the inner layer torn off as it was cut and mounted or otherwise, but it runs parallel to the main body of the inner fibers, and the middle layer terminates in the center of the specimen of the field. The inner and outer layers, which constitute the regenerated fascia, continued on for two inches or more across the defect (Fig 4B) until they came to the fascia lata margin of the opposite side where the inner and outer layers continued on in continuity with the inner and outer layers of the normal fascia lata margin and the strong middle longitudinal bundles appeared again (Fig 4C).



Fig 4B—Two layers of regenerated fascia lata.



Fig 4C—Three layers of fascia lata margin

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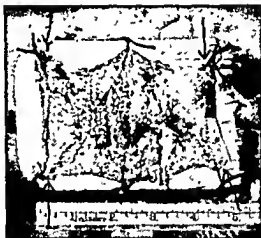


Fig 5A—Arrows point to narrow normal fascia lata margins, the wide intervening material is regenerated fascia lata

An incision was made longitudinally parallel with the long axis of the defect along the mesial edge of the normal fascia lata, taking 1 cm. of that edge for a distance of three and one half inches. A similar incision was made in the external shelf. A transverse incision was made at the ends of these two parallel incisions connecting them and thus freeing a block of regenerated fascia with 1 cm. of normal fascia lata attached to either side, the whole of which was three and one half inches long and four inches wide. This regenerated fascia stripped off the muscle with the same ease as did the normal fascia lata. Grossly it had a visible capsule or sheath on its internal and external surfaces, of a glistening, grayish white color, which was in direct continuity with that of the normal fascia lata on both surfaces. The external surface contained a few tags of fat as did the normal fascia lata. The inner surface had a few fine trabeculae and small blood vessels extending to the muscles as did the normal fascia lata. Two long fascia strips three eighths inch wide were taken from the remaining part of the lateral shelf of normal fascia lata to repair the hernia. (One of my colleagues, a former naval medical officer in World War I, who is marine minded, saw this specimen and remarked, "Now you have a specimen from shore to shore.")

In Fig 5A is shown the gross specimen of regenerated fascia lata with a narrow rim of normal fascia lata on each side. The cutting of this specimen was ingenious and it was



Fig. 5B—Left three-fourths is normal fascia lata margin with its three layers. The right one-fourth is the beginning of regenerated fascia lata, two layers



Fig. 5C—The two layers, inner and outer transverse, of the regenerated fascia lata.

cleverly mounted so that the full width of the specimen cut transversely was mounted in continuity on one large piece of glass, thus allowing microscopic study of the specimen from one end to the other. In Fig. 5B are shown the normal fascia lata margin of one side of this huge specimen with its three layers of fibers and the beginning of the regenerated fascia on the right comprised of its two usual layers, namely the inner and outer. In Fig 5C is shown the continuation of these two layers for three and one half inches until the other margin of normal fascia lata is reached with its three layers on the right (Fig 5D)



Fig 5D—The three layers of normal fascia lata margin in right half

#### CONCLUSIONS

1. Regenerated fascia lata contains two layers, an inner transverse and an outer transverse layer. These two layers are in continuity with, and are direct extensions of, their corresponding layers of normal fascia lata which extend across the defect regardless of its size. Occasionally the transverse fibers do not run exactly at right angles to the longitudinal fibers. During an operative procedure when the fascia lata is dissected out, if one will observe carefully, the transverse layers will sometimes be seen to run somewhat obliquely to the long axis of the thigh. But the direction of the longitudinal fibers is constant.
2. It is never necessary to suture layers of fascia lata across the defect from which a transplant has been taken, or to make any effort to repair by one way or another the defect to prevent herniation. Herniation will be prevented by the newly formed regenerated fascia.
3. The more active is an individual, the more dense and better developed will be the regenerated fascia lata.
4. Regenerated fascia lata of six months to one year of age will be of sufficient density and tensile strength to be used successfully in certain surgical procedures in which, ordinarily, normal fascia lata is desired but lacking.
5. At first thought this work might appear to substantiate the work of Gratz<sup>2</sup> that fascia will develop anywhere in the body from muscle where fascia



is needed. In every instance of this work it is shown that the regenerated fascia layers are direct extensions across the defect of those corresponding layers of adjacent normal fascia lata. But the noticeable prominence of the thickness and density of the inner layer over that of the outer layer strongly suggests the importance of the proximity of muscle to the success of the fascia regeneration.

The author is grateful to Dr. Carl V. Weller, Chairman of the Department of Pathology of the University of Michigan for his personal attention to the cutting of the blocks of these specimens, and to Miss Evelyn Irvine of his Department for the mounting and final preparation of the slides.

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## ACUTE SUPPURATIVE PHLEBITIS COMPLICATED BY SEPTICEMIA

HAROLD NEUHOF, M.D., AND GABRIEL P. SELEY, M.D., NEW YORK, N. Y.

(From the Surgical Service and the Department of Laboratories, the Mount Sinai Hospital)

AS A CONSEQUENCE of the extraordinary results which are so often obtainable in the treatment of septicemia by the use of penicillin and of the sulfonamide drugs at this time there is an inevitable tendency to pay little or belated attention to lesions amenable to surgical relief. Among the latter is suppurative phlebitis of venous trunks. It may, therefore, be timely to present a study of this lesion based on ninety-three cases, the preponderance of which are certified instances. The importance of suppurative phlebitis as the feeding focus for septicemia was shown in its occurrence in one-fifth of 400 unselected cases of pyogenic sepsis<sup>1,2</sup>. The extremely high mortality of unrecognized or untreated suppurative phlebitis which existed under such circumstances was an obvious challenge to diagnosis and therapy. Some influence on the mortality rate by operative treatment of suppurative phlebitis was demonstrable<sup>3</sup> in the period before, as well as in the earlier phases of specific chemotherapy. The question remains as to the role of surgery in the present phase of therapy by sulfonamide drugs and more particularly by penicillin. For its evaluation, more difficult than before, a full knowledge is required of the pathology, bacteriology, and clinical manifestations of suppurative phlebitis when complicated by septicemia.

It should be stated at once that the pathology of acute phlebitis uncomplicated by sepsis may be identical with that found in phlebitis from which septicemia is derived. Cases lacking all or many of the features of septicemia are not under consideration in this instance. There is also omitted an unusual but important group of cases of bland thrombosis characterized by chills and fever amenable to cure by venous ligation with or without thrombus extraction (to be reported elsewhere). The ninety-three cases will be analyzed according to etiology and pathogenesis, clinical pathology, bacteriology, topography, diagnosis, operative indications, and treatment.

### ETIOLOGY

In the great majority of cases there was demonstrable a suppurative or acute inflammatory (often phlegmonous) focus in the immediate region of the large venous trunk which was the seat of phlebitis. It was a reasonable assumption that such foci (frequently suppurative lymphadenitis) were the sites from which the phlebitis was derived. These foci of infection were in turn derived from some more removed source of entry of infection into the body. Thus, a typical sequence of events was infection of a finger, lymphangitis of the arm, subpectoral suppurative lymphadenitis, suppurative thrombosis of the axillary vein, and septicemia. There are, of course, many instances in which such a clean-cut sequence of events is not apparent but some evidence of the etiologic relationship was to be found in almost all the cases in our series. It may be

well to restate that we are concerned solely with phlebitis of substantial venous trunks. Phlebitis of venous radicles and often of small veins can be regarded as a part of the picture of any suppurative or phlegmonous lesion virtually anywhere in the body, is not recognizable as such clinically, and is not here under consideration.

The cases in our series are unselected and are listed as they occurred in a general hospital. As a result there is a considerable variety of venous trunks which are involved. The sites of suppurative foci from which main trunk phlebitis was derived also varied but can be placed in four groups (Table I).

Special attention should be called to a group of six cases in which suppurative phlebitis and sepsis followed either a cut-down intravenous infusion or repeated or prolonged intravenous infusion at a single site. It may be agreed that most of these patients were seriously ill and presumably prone to develop infection from an ordinarily trivial source. However, the infection is preventable by avoiding prolonged intravenous therapy at any one site. If the latter is unavoidable, the prophylactic administration of sulfonamide drugs or penicillin is warranted. In any event, the danger of septicemia from prolonged intravenous therapy at a single site should be acknowledged and combated.

TABLE I SITES OF SUPPURATIVE FOCI FROM WHICH MAIN TRUNK PHLEBITIS WAS DERIVED

SITE	NUMBER OF CASES
In soft parts chiefly of extremities and neck	43
In region drained by the portal system	20
Otitic	20
Miscellaneous	10
Total	93

Another small but important group of cases, three in number, were those of phlebitis related to infections of long bones. Drainage of the abscess of the soft parts and of the bone in these cases did not influence the unfavorable clinical course inasmuch as suppurative phlebitis of substantial venous trunks was present in these cases. They are noted here because of the etiology and pathogenesis of the phlebitis.

In our series the etiology and pathogenesis was well illustrated by the appendiceal cases, six in number. In sequence to acute appendicitis there was a mesenteric abscess and phlebitis of the appendiceal veins which extended into the terminal branches of the ileocolic vein. From this area could be traced phlebitis of the superior mesenteric veins extending into the portal. The further sequence was liver abscesses, occasional phlebitis of the hepatic vein, and in some of the cases phlebitis of the inferior vena cava, abscesses of the lung, and pulmonary vein phlebitis with metastatic abscesses in the distribution of the systemic circulation.

Thus, the etiology of septicemia in all the cases of phlebitis of main venous trunks, ninety-three in number, was the phlebitis. The corollary was that cure could not be achieved unless the infected area of the vein was eliminated.

There was no demonstrable etiology for the suppurative phlebitis, such as an abscess in the soft parts, in only two of our cases. In both of these the femoral

and iliac veins were involved. Since all the other cases presented a more or less obvious etiology either during life or at autopsy, these two exceptions are worthy of some discussion. It would lead too far afield to discuss the subject of bland venous thrombosis (phlebothrombosis) in the lower extremities but we may state here that occasional cases presumed to be in this category proved to be cases of septic phlebitis. We shall report elsewhere that cultures of thrombi proved to be positive for pathogenic organisms in some of the cases of apparently bland thrombophlebitis. Finally, we have had the opportunity to follow the course in one case from bland thrombosis into extensive suppurative phlebitis of the popliteal and femoral vein. It will be noted that our only two cases of unknown etiology were femoral vein suppurative thrombosis. In the absence of other evidence we assumed that they represented the conversion from bland thrombosis of the lower extremities with that obscure etiology which characterizes other cases of venous thrombosis of the lower extremities.

#### CLINICAL PATHOLOGY OF SUPPURATIVE PHLEBITIS

An analysis was made of the reports on the infected veins filed in the Department of Laboratories with special reference to surgical implications. The specimens were obtained at operation or at autopsy. Obviously in the case of the former only limited study was possible. In the series of ninety-three cases only three without specimens were included. They were clearly cases of suppurative phlebitis, clinically and at operation.

It can be assumed that phlebitis of substantial venous trunks is derived from extension from smaller branches or from immediately adjacent suppuration. However, the pathway of the extension can be demonstrated only rarely. The gross pathology of acute infections of venous trunks is varied. We believe the lesions can be grouped into four characteristic macroscopic forms as follows:

1. The thrombophlebitic. A lustreless more or less thick-walled vein is expanded about its contained, often palpable, thrombus. The lesion usually is well circumscribed with a visible demarcation from adjacent normal vein. The length of the area of suppurative thrombophlebitis ranges from one-half inch to several inches or more. In the case of portal vein phlebitis the contents may be gangrenous and foul-smelling debris. However, the appearance in any case may be altered as the result of chemotherapy or penicillin. Thus, in a recent case of suppurative thrombophlebitis of the portal vein, the wall of the vein was considerably thickened and the contents were some fluid pus and firm, fleshy, thrombotic material.

2. The phlegmonous. The wall of the vein is grayish, hemorrhagic or necrotic, and is infiltrated. A visible thrombus may not be present. The lesion usually has an ill-defined limit.

3. The pyophlebitic. The wall of the vein usually shows only slight evidence of inflammation and at times so little that the discovery of pus within it is unexpected. The limits are ill-defined. In addition to fluid pus, small bits of thrombotic material may be found within the lumen.

4. The periphlebitic. The venous trunk is more or less embedded in inflammatory tissue. The wall of the vein is thickened, for the most part lustreless,

and may or may not contain a palpable thrombus. Usually it is difficult to determine if the change in the vein represents the alteration in the surface of any structure in contact with an inflammatory process or a phlebitis with or without thrombus involving all the coats of the vein.

The microscopic examination does not match the foregoing gross features. Although there are many variations in the picture, two main varieties can be described into which the cases can be grouped:

1 *Acute suppurative phlebitis or suppurative thrombophlebitis*; 84 per cent of the cases

2 *Acute phlebitis, endophlebitis, periphlebitis*; 16 per cent of the cases

With appropriate stains, bacteria can be discerned in varying numbers in the thrombus or in the walls of the infected veins. Indeed, the absence of bacteria should cast grave doubt in any given case as to septicemia having been derived from an infected venous trunk submitted to microscopic examination.

An analysis of our cases reveals extensive spread of suppurative phlebitis which usually takes place toward the later stages of the infection and as found at autopsy. In some of the patients operated upon relatively early in the stage of septicemia (or in a few instances in the pre-septic stage) the suppurative phlebitis was sharply limited. Apparently the area of infection in the vein spreads rapidly in the middle and later stages of the disease. On the basis of a few observations it may be stated that in the case of portal vein phlebitis the lesion may be extensive even in the early stages of septicemia.

A study was made of the relationship, if any, between the types and extent of the pathology in the vein and clinical manifestations. In general no direct relationship could be discerned, although it can be said that the classical or typical picture of septicemia was most often seen in suppurative thrombophlebitis. Furthermore the blood culture features—positive or negative blood culture, number of microorganisms, variety of bacteria—bore no apparent relationship to the extent or severity of the phlebitic process.

Some aspects of the pathology are worthy of special mention because of their surgical implications. There were two cases in which the source of infection was adjacent to the axillary vein which, however, was by-passed or skipped, the subclavian vein being the seat of the phlebitic process. Perhaps the fulminating and rapidly fatal course in both cases was related to the unusual pathway of extension. In a case of suppurative pylophlebitis derived from an appendicitis, the superior mesenteric vein was by-passed. Thus, the possibility that phlebitis may skip a substantial or main venous trunk to be present at a more central and larger trunk must be borne in mind in order to avoid overlooking the lesion at an operation.

Phlebitis of a main venous trunk apparently derived from a crosscurrent infection may also occur. There was one striking instance in which the left renal vein was involved following a phlebitis of the right renal vein complicating a carbuncle of the kidney. This case also illustrated the fact already alluded to that severe phlebitis without thrombosis can occur and that the surface of the vein may not reveal a marked change in appearance.

When a branch close to a venous trunk is involved by phlebitis, extension to the parent vein can be regarded as virtually inevitable unless an operation is performed at an early stage of the infection and terminates the branch phlebitis. There was one case of branch vein suppurative thrombophlebitis in our series in which the inflammatory process seemed to terminate just short of the axillary vein. The gross appearance of the axillary vein was normal in this case. Since excision of the infected branch vein also resulted in cure and the vein at the site of section close to the axillary vein was normal, it is assumed that the phlebitis had not extended into the axillary vein.

#### BACTERIOLOGY IN RELATIONSHIP TO PROGNOSIS

The great preponderance of our cases antedates the period of chemotherapy and penicillin. The series should, therefore, be useful for comparative purposes. Blood cultures were taken in eighty-six of the ninety-three cases and were positive in fifty-four (Table II). The microorganisms found in the latter are grouped in Table III. The bacteria other than streptococci, and staphylococci included *Bacillus coli*, Friedlander's bacillus, *Streptococcus viridans* and enterococcus. Anaerobic bacteria were recovered in four instances and there were three cases in which two microorganisms were present in the blood stream.

TABLE II. ANALYSIS OF THE RESULTS OF BLOOD CULTURES IN 86 CASES, RELATIONSHIP TO MORTALITY

BLOOD CULTURES	NUMBER OF CASES	NUMBER OF DEATHS	MORTALITY PER CENT
Positive	54	37	68.5
Negative (portal vein phlebitis in 7 of these)	32	17	53

Evidence of septicemia at autopsy in all fatal cases of both groups

TABLE III. MICROORGANISMS IN FIFTY FOUR POSITIVE BLOOD CULTURE CASES

ORGANISM	NUMBER OF CASES	NUMBER OF DEATHS
<i>Streptococcus hemolyticus</i> (beta)	24	10
<i>Staphylococcus aureus</i>	13	12
Other microorganisms	17	15

The group of seventeen cases of portal vein phlebitis in which blood cultures were taken provides some special features. The blood culture was positive in ten of these cases. This high percentage is not in keeping with commonly held concepts which maintain that filterage by the liver commonly prevents general systemic invasion by the infecting organism. It is also maintained that a phlebitis of the hepatic vein should be postulated in cases of pyelephlebitis in which the blood cultures are positive but hepatic vein phlebitis was not found at post-mortem examination in a number of our cases.

Negative blood cultures in pyelephlebitis may be in the same class with negative blood cultures in suppurative phlebitis in systemic venous trunks. The latter, in the presence of evidence of septicemia (clinically or at autopsy), cannot be accounted for in an offhand manner. Indeed, there appears to be a school which believes and teaches that septicemia cannot be regarded to exist in

the absence of a positive blood culture. Thus, in the field of phlebitis of the lateral sinns there are those who believe that the diagnosis cannot be regarded as established or at any rate that surgical intervention is not indicated until a positive blood culture is obtained. It is, of course, fair to assume that if sufficient cultures are taken at frequent enough intervals microorganisms would be found in the blood stream in all cases. Table II is, therefore, of important clinical significance because it reveals the high proportion of negative blood cultures taken in the standard manner and with good technique in proved cases of phlebitis complicated by septicemia. It can be added that the mortality of this group would have been higher if some of the patients had not been cured by operation. If filtration by the liver does not explain negative blood cultures in suppurative pybphlebitis, what explanation can be offered for negative blood culture in suppurative phlebitis of systemic venous trunks? It appears to me to be logical to assume that the variety of phlebitis accounts for the presence or absence of bacteria in the blood. We believe that the type of phlebitis characterized by more or less obliterating thrombosis or by "fleshy" and firmly adherent thrombi is the form or one of the forms in which blood cultures are likely to be sterile. It also appears reasonable to believe that blood cultures are more prone to be positive when the vein which is the seat of phlebitis is in a direct line with the flow of the blood stream rather than in an eddy or in a situation in which the venous pressure is high rather than low. In general, the nearer the heart the more definitive the suction action on the venous trunk, which is the seat of thrombosis, and the more one would anticipate a positive blood culture.

A study was made in order to learn if there were any correlation between the severity and extent of the phlebitis and the blood culture results. No correlation was found to exist. Thus, blood cultures were negative in not a few instances of the severest forms of suppurative thrombophlebitis. There was also no relationship between the number of colonies in cases of positive blood cultures and the extent of the lesion or the prognosis. As shown for septicemia in general,<sup>1</sup> there is to be noted in septicemia derived from suppurative phlebitis of venous trunks that fulminating cases may have few colonies and cases pursuing a relatively bland course may have many or even innumerable colonies.

#### TOPOGRAPHY

An analysis of the sites at which suppurative phlebitis was located in the ninety-three cases shows that a great many are readily accessible surgically

TABLE IV. ACCESSIBLE VENOUS TRUNKS INVOLVED BY SUPPURATIVE PHLEBITIS IN 43 CASES (OTTIC OMITTED)

Axillary vein	12
Other veins of upper extremity	7
Veins of lower extremity	8
Internal jugular vein	5
Other veins of neck	3
Facial vein	2
Iliac vein	2
Ovarian vein	1
Other veins	13

and that the continuity of none of the venous trunks (with the possible exception of the portal vein) was essential to life. Omitting the groups of lateral sinns and portal vein phlebitis, the readily accessible veins, situated chiefly on the surface of the body, are listed in Table IV. The large proportion of cases in which relatively simple surgical procedures can aid in the solution of the problem of septicemia thus becomes apparent.

#### DIAGNOSIS—OPERATIVE INDICATIONS

A diagnosis or presumptive diagnosis of suppurative phlebitis of a venous trunk as the cause of septicemia can be made in most instances, chiefly on indirect evidence. However, the diagnosis usually cannot be entertained in the absence of a determinable source of infection. It is, therefore, of interest to note that a definite source existed in eighty-three of the ninety-three cases (Table V). Usually the inflammatory mass or abscess was in the region of, or more often in juxtaposition to, the infected venous trunk (seven-eighths of the cases).

TABLE V. CLINICAL FEATURES POINTED TO AS THE SOURCE IN EIGHTY-THREE CASES

	NUMBER OF CASES
Abscess or area of suppuration	16
Inflammatory mass or cellulitis	10
Inflamed vein palpable as such	5
Mastoid or other osseous focus	32
Portal system: chiefly cholecystic or appendiceal foci	14
Subpectoral abscess or mass (special mention because of its importance and frequency)	9

The general clinical manifestations are those of septicemia and as such are not distinctive of phlebitis as the source. An analysis of the manifestations has already been made<sup>1,2</sup> but was repeated for this series of cases. The classical febrile course was present in only one-half of the cases and chills occurred in only two-thirds of the cases. The blood culture was positive in five-eighths of the cases.

From the foregoing it appears that the diagnosis of suppurative phlebitis of a substantial venous trunk should be entertained in the presence of septicemia when a likely etiology exists and the inflammatory or suppurative focus is situated in the neighborhood of, or in immediate proximity to, such a venous trunk. We maintain that under certain circumstances to be set forth, surgical exposure for diagnosis and, in the presence of phlebitis, excision of the infected vein are warranted. In this connection the frequently made diagnosis of complicating bacterial endocarditis should be referred to since that lesion forbids surgical intervention because of its futility under such circumstances. We would emphasize the fact that the diagnosis cannot be made on the presence of heart murmurs and positive blood cultures, or even petechiae which may be of bacterial or non-bacterial origin. In any event the margin of error in the diagnosis of bacterial endocarditis is great and if an operation is indicated it should not be withheld unless the diagnosis of endocardial invasion is virtually certain.



## INDICATIONS FOR OPERATION FOR SUPPURATIVE PHLEBITIS

In the period before sulfonamide and penicillin therapy the indications for operation were both precise and urgent in our opinion. The requirement was to eradicate if possible, and at the earliest moment, the area of the infected vein from which septicemia was derived. Indeed, the best results were obtained, as might have been anticipated, by operations performed in what may be called the preseptic phase or at any rate before sepsis was fully established. The indications now are profoundly influenced by sulfonamide and penicillin therapy since many cases will not require operation because cure is achieved by such therapy. Operation now is indicated only in those cases in which cure is not achieved. This does not refer to the drainage of an abscess or the eradication of a suppurative focus from which the phlebitis is derived because the indications for such drainage or surgical eradication remain unchanged. Concerning the phlebitis, however, the evidence is clear that healing will result so often that sulfonamide, and more particularly penicillin, treatment can be referred to as specific therapy in most cases. The important point today in the treatment of suppurative phlebitis which has produced septicemia is to identify in good time the patients who do not respond to that therapy and to operate on the vein under such circumstances. Much closer clinical observation is required in order to determine the progress of the case. Blood cultures may become negative during the spread of a suppurative phlebitis. Indeed, the evaluation of the clinical state during either penicillin or sulfonamide therapy requires an approach which comprises a considerable modification of previous thinking. A lack of appreciation of the extension of suppurative phlebitis may lead to the omission of, or too long-delayed, surgical intervention.

On the other hand, partial effects of sulfonamide and penicillin therapy warrant a more deliberate attitude toward surgical intervention than existed in the past. Thus, a delay in operation in a recent case, to which reference will be made, appeared to be justified. In another case operation was seriously entertained but further treatment with penicillin resulted in cure.

## CONTRAINDICATIONS TO OPERATION

The question of general contraindication to operative treatment of suppurative phlebitis of large venous trunks warrants some discussion. The factor of bacterial endocarditis has been taken up. Otherwise the only general contraindication to be conceded is an evident hopelessness of a case because of its advanced stage. The argument that operation is not indicated unless the diagnosis of phlebitis is certain and not presumptive would result in the exclusion of most of the cases which might be amenable to surgical relief and the inclusion chiefly of cases too far advanced for surgical cure. There is the implication that a definitive operation for known phlebitis can be justified, but that an exploration of a venous trunk in the midst of an inflammatory area is meddling, may lead to untoward results, and is unwarranted. It appears to us that precise, nontraumatic surgical dissection will not open significant areas of infection and we have not noted ill effects in a number of instances of negative ex-

plorations for suspected phlebitis. In any event an appreciation of the little which might be lost compared with what might be gained in the treatment of an otherwise probably fatal condition should counterbalance that argument. A general contraindication to radical operation (excision) of the large venous trunks of the extremities rests on the assumption that considerable edema would follow. In the first place the primary assumption is false because edema is due to lymphatic blockage and not to the occlusion of a vein. Thus, many cases of ligation of the femoral vein for bland thrombosis in the lower extremities are not followed by edema. Second, excision of venous trunks may or may not be followed by edema, depending on the subsequent adequacy or inadequacy of lymphatic flow.<sup>2(4)</sup> One of us has reported<sup>2(a)</sup> a series of cases of excision of the axillary vein in radical operation for cancer of the breast in which edema of the arm did not result in the majority of instances. Third, the periphlebitis associated with most cases of suppurative phlebitis could undoubtedly be the cause of edema from lymphatic obstruction in not a few cases if recovery without operation should in fact occur.

Concerning surgical intervention on the portal vein it can be said that life is compatible with its occlusion unless closure is too abruptly induced in the normal vein because a collateral circulation can and does form rapidly.<sup>4</sup> Collateral circulation can be assumed to exist by the time operation is considered because the lesion of the portal vein usually is a more or less occluding thrombophlebitis, which has led to the opening of collateral hepatopetal vessels. Thus, ligation or drainage or a combination of both performed on the portal vein cannot be regarded as contraindicated in pylephlebitis on the basis of the danger of death resulting from the procedure.

#### OPERATIVE TREATMENT—EXCISION OF VENOUS TRUNK

It is impossible to ascertain if there is an accepted method of surgical treatment of suppurative phlebitis because of the virtual absence of any literature on the subject. Indeed, excluding operations on the lateral sinus and the ovarian vein it is only from personal communications that one can learn that any form of surgery for suppurative phlebitis has been attempted in the presence of septicemia. One of us has advocated<sup>2</sup> the principle of excision of the infected vein as the logical method of treatment but is unaware of the acceptance of that method. Ligation of the vein proximal to the site of phlebitis has been recommended but we believe this to be inadequate because the infection (and suppurative phlebitis) is not prevented from extending through collateral branches, and the suppurative focus is permitted to remain in place to spread locally at will. In the otologic field, where excision is not feasible, a compromise procedure consisting of unroofing the infected lateral sinus (with or without ligation of the jugular) often has yielded satisfactory results. Simple proximal ligation may produce results which were unobtainable before because of sulfonamide or penicillin therapy. This does not seem likely to us, however, as operation will probably be indicated because (1) the suppurative phlebitis does not respond to that treatment at which time excision, whenever feasible, is indicated or (2) the septicemia is controlled but the phlebitic area is converted into a

collection of pus and exudate from which infection continues and for which ligation would be ineffective. Under these circumstances drainage may be indicated rather than excision, particularly when excision is a formidable procedure. Only drainage could, of course, be considered when excision is not possible as in the case of pylephlebitis.

Some principles for excision of infected venous trunks appear worthy of note even though the procedure is indicated less frequently than heretofore. Adherence to them has yielded a measure of good results in the past and they are equally applicable today, in our opinion. Perhaps the most important principle is not to be satisfied with the drainage of a collection of pus in the neighborhood of an accessible venous trunk when the clinical picture points strongly to septicemia. The first principle then is the exposure of the vein in question by precise surgical dissection at or in the area of infection. The exposure should be liberal but should extend through normal planes only enough to reveal a normal portion of the suspected vein. The dissection of the vein is then continued through the area of infection, the vein often being embedded in inflammatory tissue or exudate. The next principle is perseverance in the dissection of the vein throughout most or all of the area in which it is embedded with severance of intervening structures (muscles, etc.) if necessary. Only by means of such a dissection will limited thrombophlebitis or phlebitis with relatively insignificant external alteration be discerned. Complete dissection of the vein into normal areas at both ends and complete excision whenever possible comprises the third principle. Only by complete exposure can the limits of phlebitis be identified and thrombosis involving branches of the parent trunk cared for. Complete excision should be carried out whenever feasible regardless of the size or importance of the venous trunk—for example, excision of the subclavian into the innominate vein—because timely eradication of the lesion will cure the septic state.

#### RESULTS OF OPERATIVE TREATMENT

Operative treatment of some sort was employed in forty-three cases (lateral sinus cases are omitted) in which suppurative phlebitis of accessible veins existed. All cases are included whether or not operation was performed on the infected vein. In Table VI is revealed the significant fact that operations limited to drainage of the suppurative focus from which the phlebitis was derived were never followed by recovery. The contrast between the futility of drainage without surgical treatment directed toward elimination of the phlebitic focus and the results of combining both, particularly when adequate excision of the vein was

TABLE VI

	CASES	RECOVERED	DIED
I. Excision of veins in addition to drainage of causative abscess			
A. Adequate excision in accordance with described technique	16	14*	2
B. Inadequate excision or excision late in the disease	15	8	7
II. Operative procedures on the suppurative foci but not on the involved veins	12	0	12

\*One patient died subsequently of an unrelated disease

performed, also is apparent in the table. This conclusion today would probably hold only for cases in which the infection in the vein was not amenable to drug therapy. The twenty cases of phlebitis of the sigmoid sinus are omitted because their analysis requires considerations related only to the otologic field. It is interesting to note, however, that good results were obtained in this field in which the management of the problem of phlebitis is much more difficult than in general surgical fields and that radical excision which at least at times can be carried out elsewhere cannot be performed safely on the lateral sinus.

With emphasis on the fact that this study is based solely on phlebitis of major venous trunks we report the results of therapy by sulfonamides in our series of cases despite surprisingly poor results (Table VII). The number of cases is not large and better results might be anticipated in a larger or perhaps more representative series. All cases in which sulfonamides were not administered in adequate dosage are excluded. The apparent lack of any significant relationship between the blood culture findings and the results will be noted.

TABLE VII. THE INFLUENCE OF SULFONAMIDE THERAPY IN FOURTEEN CASES OF PHLEBITIS OF MAIN VENOUS TRUNKS COMPLICATED BY SEPTICEMIA

BLOOD CULTURE	NUMBER OF CASES
Positive	8
Ineffective in all	
Negative	6
Ineffective in 4	
Questionable efficacy in 2	

The results of excision in relationship to the blood culture and pathology of the infected vein can now be tabulated (Table VIII). Here again the series is not large and different results might be obtainable in a larger and more representative series or one in which excision had been carried out more promptly than was possible or deemed advisable in this series. The table also shows that there is slight relationship of the pathology or the findings on blood culture to the results which were achieved. The prognosis of suppurative phlebitis of main venous trunks complicated by septicemia appears to be related largely if not solely to the duration of clinical manifestations at the time of operation and to the accessibility of the infected vein and feasibility of adequate surgical treatment.

Reference has been made to the profound influence penicillin has had on the problem of sepsis producing phlebitis. Up to the present time we have seen

TABLE VIII. PATHOLOGY AND BLOOD CULTURE IN RELATIONSHIP TO THE RESULT

	CASES	RECOVERIES	DEATHS
Positive blood culture			
Suppurative phlebitis	4	2	2
Negative blood cultures			
Periphlebitis	3	3	
Suppurative phlebitis	6	6	
No specimen	1	1	
Blood culture not awaited before operation			
Postoperative culture negative			
Suppurative phlebitis	2	2	

no instances in which cure has not been achieved when the infection is amenable to penicillin therapy. Penicillin has proved to be far more effective than the sulfonamides and the foregoing statistics (Table VII) would almost certainly have been far better had the patients been treated with penicillin. It is, however, apparent that, as in the case of the sulfonamides, there will be cases of failure or partial results by penicillin therapy, in which operation on the vein will be indicated. In a recent case of pylephlebitis (not in this series) sulfonamide therapy was employed over a long period of time. There was improvement in the clinical course (and negative blood culture) despite the known presence of suppurative hepatic foci. Finally, operation was performed on the portal vein consisting of drainage of pus from the lumen. Parallel experiences with parallel operative indications and procedures in the case of penicillin can be anticipated.

#### SUMMARY AND CONCLUSIONS

1 In the prepenicillin period, suppurative phlebitis was a common cause of fatal septicemia; in the present period it is often in an abortive form because of penicillin therapy. Suppurative phlebitis remains the common cause of septicemia.

2 The diagnosis of suppurative phlebitis producing septicemia often must be made on indirect evidence: an inflammatory focus (present in seven-eighths of the cases), chills (in two-thirds of the cases), and positive blood culture (in five-eighths of the cases).

3. Drainage of the suppurative focus will not suffice unless there is added thereto adequate excision of the main involved venous trunk. The combination of these procedures resulted in cure in 87.5 per cent of cases.

4 In the penicillin (and sulfonamide) era, fewer cases will be encountered in which surgical considerations will arise. In penicillin-resistant cases or in cases of partial results, the same principles of surgical treatment which have been laid down should be applied.

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## THE AMBULATORY TREATMENT OF PHLEBITIS, THROMBOPHLEBITIS, AND THROMBOSIS WITH COMPRESSION BANDAGES

OTTO MEYER, M.D., New York, N. Y.

**T**REATMENT of acute and chronic phlebitis with pressure bandages has been very successful and has been in use in nearly all European countries for two decades.

Compression bandages have been recommended by many authors for the treatment of thrombosis and the prevention of pulmonary embolism. Castleman, from autopsy studies, has found the source of pulmonary embolism to be in the deep veins of the legs in approximately 95 per cent of the cases.

Lately compression bandages have been used in this country prophylactically. Ochsner stated, "There is only one treatment for pulmonary embolism and it is prophylaxis. A great deal can be accomplished by preventing the clot originally, as the authors have emphasized. It is my belief that every patient past 45 years of age who has to be operated on should have his extremities wrapped from his toes to his groin before he goes to the operating room. This wrapping is maintained during his postoperative period until he is able to move his extremities actively. Early ambulation has undoubtedly done a great deal to cut down the incidence of postoperative thrombosis."

Peripheral phlebitis is located chiefly in the legs, because the mechanism of the venous circulation favors infection of the veins of the legs. To meet the problems involved in the treatment of peripheral phlebitis we must have a clear conception of the factors which force the venous blood to flow back to the heart.

Besides the contraction of the left ventricle, the vis a tergo, and the negative pressure within the chest which sucks the venous blood into the thorax, the massaging effect of the skeletal muscles is of utmost importance. The pressure of the contracting muscles on the veins pushes the blood to the heart, because the valves of the veins permit movement of the blood only in this direction and prevent its backflow to the tissues. The muscles, therefore, act as subsidiary pumps which aid materially the flow of the venous blood, especially during muscular exercise.

The effect of muscular exercise on the venous flow can be demonstrated easily in bloodletting from the vein in the elbow. The blood flows more freely when the patient opens and closes his fist, thus exercising the muscles of the forearm. Each contraction of these muscles exerts a pressure on the underlying veins and increases the flow of venous blood to the opening of the needle.

But in spite of increased muscular contraction of the forearm muscles, much pressure energy is lost into the empty space. I was able to demonstrate how a materially increased venous flow can be achieved by application of elastic

bandages around the forearm. After the bandages are firmly (naturally centripetally) applied, all the pressure energy can be concentrated on the deep veins.

If there is insufficient activity of the skeletal muscles of the legs, as in persons who stand much during their working hours, or who do little walking, a venous congestion develops in the legs and creates a *locus minoris resistentiae* to infection.

It is well to note that Krogh has pointed out that a relatively small elevation of venous pressure must cause fluid to accumulate in the tissue spaces. An example of this is that the erect human being is constantly near to edema.

Then, when the veins have become infected, the venous congestion becomes permanent and more pronounced. The inflammatory swelling of the inner coat of the veins and the formation of blood clots decrease the diameter of the veins. A permanent phlebostenosis develops which decreases the capacity of the veins to carry a normal volume of blood from the tissues to the heart, thus producing a permanent venous congestion in the affected area which weakens the tissues to such an extent that they cannot overcome the infection.

The tissue in an area of venous congestion is affected by retardation of the circulation which results in accumulation of carbon dioxide, accumulation of metabolites, and stagnant anoxia.

When the capillary walls are exposed to oxygen lack, in the frog even for as short a time as three minutes, they are damaged and become permeable to protein.

Impairment of venous drainage increases venous pressure which results in increased transudation into the tissue spaces. Increased pressure in tissue spaces creates pain by compressing nerve tissue.

The local effect of stagnant anoxia is often responsible for necrosis and ulcer formation in a congested area.

Allergic reactions, according to Knepper, are especially severe in a congested area with retarded circulation. The interaction between antigen and antibody is dependent on the time factor. In a congested tissue, therefore, we find allergic reactions of the skin in the form of congestive dermatitis and congestive eczema.

As the venous congestion is the principal factor which prevents the elimination of the infection from the veins, the customary method of treating phlebitis is useless, because it does not attack the venous congestion. Removal of the venous congestion is the "*conditio sine qua non*" for a cure of peripheral phlebitis. In the customary treatment of phlebitis the patient is confined to bed for a long period of time with the leg fixed in an elevated position. All that can be accomplished by the rest cure is a temporary improvement, but never a cure. Unless the venous congestion in the legs is removed, a cure is impossible.

For this reason the anticoagulant therapy, with heparin and dicumarol, and the ligation therapy have not been very successful in the treatment of thromboses and in the prevention of embolism.

In treating phlebitis of the legs two purposes must be achieved at the same time. One is to cure the phlebitis by removing the venous congestion. The other is to prevent the detachment of a blood clot. Both purposes are achieved by the use of pressure bandages.

It was the merit of H. Fischer to have originated the ambulatory pressure treatment of phlebitis. Fischer observed that in the treatment of leg ulcers inflamed superficial veins healed remarkably fast under compression bandages. This observation encouraged him to treat also the inflammation of deep veins with compression bandages.

Fischer's method was devised with the aim of eliminating embolism and progressing thrombosis. By applying a strong and even pressure around the leg to a point above the inflamed vein, he succeeded in compressing the dilated veins, thereby restoring function of the valves and normal circulation. The pressure also promotes the absorption of existing thrombi and prevents their detachment from the walls of the veins. The restoration of the circulation prevents formation of new thrombi and removes the swelling. Fischer emphasized that the action of the pressure bandage is increased manifold by walking, because the contraction of the muscles empties the veins (that have been compressed sufficiently by the bandage to restore the function of the valves) in the direction of the heart, thereby promoting circulation.

A former pupil of Fischer, I developed in 1930 a modification and simplification of the original Fischer treatment. In the treatment of acute and chronic phlebitis of the legs I used successfully for fifteen years the elastic combination bandage. I saw not a single case of embolism in a very large number of phlebitis cases. The combination bandage consists of a 4-inch wide, moist, medicated, viscous, nonsetting, zinc-gelatine type bandage (Contura bandage) and a 3-inch wide, elastic, adhesive pressure bandage (Pressoplast bandage). The elastic adhesive bandage is used for compression and grip. It has a soft, nonfray edge.

For diagnosis and treatment the patient lies on a flat table.

The diagnosis of phlebitis and thrombophlebitis of the deep veins of the leg is made by deep palpation with relaxed muscles. Ochsner stated that the veins in thrombophlebitis and phlebotrombosis are tender and sensitive to pressure. Healthy normal veins (for example, dorsal hand veins) can stand much pressure without any pain. It is always necessary to examine both legs, as we deal in most cases with a horseshoe phlebitis. Phlebography is not without danger and not as accurate as the diagnosis by deep palpation.

The technique of the combination bandage is as follows: After protecting ankle and knee, the physician covers the leg loosely with a contura bandage. Then, over the contura bandage, he applies a three-inch wide pressoplast bandage with strong, but nonconstricting, pressure.

The combination of the medicated contura bandage and the elastic pressoplast bandage provides an elastic compression which is adaptable to the function of the muscles and joints. The moist, viscous, antiphlogistic contura bandage does not become stiff like Unna's paste bandage, and it moves freely with the muscles. The medication in the contura bandage prevents irritation



of the skin so often seen after the direct application of the elastic adhesive bandages, and it makes a comfortable treatment, even of long duration, possible. Also, the change of the bandage is easy, as the contura bandage does not stick to the hair of the leg. Therefore, shaving of the leg is not necessary.

The application of the combination bandage (contura plus pressoplast) incorporates all the advantages of Unna's paste bandage and the elastic adhesive bandage without their disadvantages. The contura bandage remains wet and pliable under the pressoplast bandage. The soothing antiphlogistic medication of the contura bandage protects the skin and facilitates the removal of the bandage.

In treating the legs below the knee, the bandage is started directly behind the toes and is wound up to the knee. The bandages are wrapped around the leg in the direction of the heart. They must cover the foot, heel, and calf. Only the toes remain free.

In treating the thigh, the bandage starts with strong pressure as high as possible near the Poupart's ligament and is wrapped around the thigh in the direction of the knee to a point directly above the knee. In order to prevent detachment and passage of a thrombus, it is necessary to apply several layers of pressoplast bandage with maximal pressure at the upper (proximal) end of the thigh.

The knee remains, as a rule, free. If it is necessary to bandage the knee, the technique is the same as previously described. After the popliteal space has been well padded with cotton, the contura bandage is applied loosely, and then the pressoplast bandage is applied under "optimal" pressure.

The pressure must be even and the tension of the bandage must be considerable. A loosely applied bandage fails to relieve symptoms. In the pressoplast bandage the combination of the particular adhesive spread with the remarkable stretch and regain properties of the cloth makes it possible to provide the exact degree of compression and grip.

If the correct pressure has been applied, the patient will feel a relief of pain immediately. If the pressure is too strong, the patient will complain about severe pain almost immediately after the bandage has been applied. He can bear excessive pressure for only a few minutes. If the bandage is too loose, the pain which the patient felt before application of the bandage will not stop. Then more pressure must be applied.

In almost all cases of phlebitis of the legs it is necessary to apply the bandage not only to the lower part of the leg, but also to the thigh, even if there are no apparent signs of phlebitis in the thigh. Careful examination by deep palpation at the middle of the thigh will disclose in almost all cases an inflammation of the deep femoral vein. It is obvious that the inflammatory swelling of the femoral endothelium interferes with the drainage of the venous blood and produces congestion in the lower leg.

It need hardly be mentioned that this method can be applied only in cases of phlebitis where the thrombosis does not involve the large vessels of the abdomen.

The Fischer treatment is contraindicated in the very rare cases of purulent thrombosis.

After application of the bandage the patient is told to walk as much as possible, at least three miles daily, and to avoid standing.

Muscular contractions during walking result in the effect of positive pressure. Muscular relaxation during walking produces negative pressure. The alternate contraction and relaxation of the muscles create a difference in pressure which is the deciding factor for the promotion and acceleration of circulation in all blood vessels.

The bandage is changed at first every third day, and later twice weekly. The swelling decreases rapidly under the bandage, especially the often enormous edema found in acute phlebitis. In these cases the bandage must be renewed as soon as it becomes loose, if necessary daily for the first days. It cannot be stressed enough that the bandages must always fit snugly and tightly. If this rule is not observed, detachment of a thrombus with subsequent pulmonary embolism may result.

Pain disappears as a rule immediately on application of the bandage, or at least decreases considerably. There is practically no danger of embolism if the bandage is applied with sufficient pressure and up to a point above the thrombus.

The modified Fischer treatment with the contura and pressoplast bandages is effective in acute, chronic, and latent phlebitis, and in their complications, namely, phlebotic ulcer and phlebotic eczema. It also is effective in most cases of varicose ulcer and varicose eczema, because varicosity is mostly complicated by a latent phlebitis in the deep veins, and the pressure bandage will remove the congestion in the legs.

In treating ulcers and eczemas of the leg with the modified Fischer treatment, the ulcer or eczema is covered first with a suitable ointment (cod liver oil) and a piece of gauze. Then the contura and pressoplast bandages are applied as described previously.

The results with the ambulatory pressure treatment, based on Fischer's principles, have been confirmed by Wright and many other authors.

H. Fischer reported in 1924 that he had treated 2,400 patients with phlebitis without a single embolism.

E. Fischer, the son of the originator of the treatment, treated 2,000 patients with phlebitis and thrombophlebitis without a single case of embolism.

Eichenlaub reported in 1931 that he had treated several hundred patients with thrombophlebitis with the Fischer method without a single case of embolism.

Stotzer treated over 1,000 patients with phlebitis with compression bandages and did not have a single case of embolism.

Leun reported in 1941 that in the Gynecological and Obstetrical Clinic of the University of Giessen after the systematic prophylactic application of pressure bandages (in 1933), 6,033 maternity patients were delivered without a single fatal case of embolism, and that 7,034 gynecologic patients were operated

upon with only twenty-two (3.1 per thousand) deaths from embolism, representing a decrease of over 50 per cent of the mortality rate from embolism as compared with the period before the prophylactic treatment with pressure bandages was introduced.

Kretschmar reported in a lecture on phlebitis at a meeting of the Hollywood Academy of Medicine in 1930 that during the past nineteen years he treated a large number of phlebitis patients in accordance with Fischer's directions without one fatal issue and without one case of embolic pneumonia.

Fischenlaub stressed the following advantages of the Fischer treatment: shorter hospitalization, no necessity of rest in bed, prompt relief of pain, shorter duration of disability, avoidance of the complications seen in cases of thrombosis which have been healed by rest in bed, such as blood and lymph congestion, ulcerated legs, inflammatory changes of the joints, flabbiness of all the muscles and ligaments. He further mentioned it as useful in preventing thromboses if used before delivery and operations, or also directly afterward. He stated that the compression restores the function of the valves of the veins, increases the compression and suction effect of the contractions and relaxations of the muscles in motion, and induces and increases the circulation.

He stressed the necessity of early treatment in order to obtain good results. The advantages of this treatment are: the patient is completely cured (*restitutio ad integrum*), and he can immediately leave the bed and walk around. Slight increases in temperature due to the thrombosis are no contraindication. The compression must be firm enough, then the pain is immediately relieved. If there was fever at the start of the treatment it will soon disappear. If it is necessary for the patient to stay in bed because of another condition, active and passive leg exercises are necessary several times daily, in order to prevent spreading of the thrombosis and also to effect a cure which, however, will take more time to effect than if the treatment is ambulatory. If the thrombosis has already spread into the abdominal cavity, the patient must at first stay strictly in bed with the legs elevated. After a period of time which varies individually in every case, a compression bandage can be applied to the abdomen in order to shorten the duration of the rest in bed. The ideal of all therapy, *cito, toto, jucunde*, is also, and especially so, the ideal of pressure therapy.

Hohmann recommended the pressure bandage treatment of thrombophlebitis very highly and believed in time every physician will use it.

The fact that the venous congestion creates a *locus minoris resistentiae* to infection in the veins of the legs makes it imperative to prevent reinfection from sources of infection elsewhere in the body while treating the peripheral phlebitis locally with pressure bandages.

In my paper on "Latent Phlebitis as a Cause of Rheumatism" I stressed the importance of oral infections as a cause of jugular phlebitis and peripheral phlebitis.

It has been proved pathologically by Dietrich, Siegmund, and Hall that acute infections spread from tonsils, teeth, and the pharynx to the jugular veins by way of the small connecting veins, establishing a secondary focus in the jugular veins.

To cure phlebitis in the legs the physician must eliminate infectious foci in the mouth cavity, as infected (especially pulpless) teeth and infected tonsils. I pay special attention to infected tonsil stumps. Since a great number of tonsillectomies are done incompletely, the physician should always think of this possibility. I had infected tonsil stumps removed in over 500 phlebitis patients. This procedure shortened the treatment of phlebitis in each case considerably.

In a paper on the eliminating function of the tonsils for dental infections, I explained how removal of infected (especially pulpless) teeth may clear up a coexisting tonsillitis.

After removal of the primary oral foci the secondary focus in the jugular veins disappears sometimes immediately without further treatment. The diagnosis of jugular phlebitis is dependent on tenderness of the jugular veins. On deep palpation sometimes an induration is felt by the palpating finger. If the infection in the jugular veins persists, leech treatment has proved successful in removing the secondary focus. I have used this method nearly daily since 1937.

In numerous papers I have emphasized the importance of removing the primary oral foci of infection and the secondary focus in the jugular veins for the treatment of peripheral phlebitis.

Removal of the primary and secondary foci is also one of the surest measures to prevent peripheral phlebitis. Ochsner and DeBakey stated, "Infections are contributory in the production of distant thromboses, because of the changes in the blood constituents resulting from destruction of tissue. For this reason, it is prophylactically desirable to remove all foci of infection whenever possible."

I agree with Robinson, who stated, "Pulmonary embolism rarely occurs unless some sort of phlebitis, usually phlebothrombosis, exists. The real prevention of embolism therefore resolves itself into prevention of phlebitis."

#### SUMMARY

The successful treatment of peripheral phlebitis hinges on one factor mainly, the elimination of the venous congestion in the affected area.

The venous congestion of the leg is eliminated by the ambulatory treatment.

The ambulatory treatment consists of the application of pressure to the leg with the combination bandage (contra plus pressoplast), and regular daily walking exercises.

The treatment cures the phlebitis in the leg by eliminating the venous congestion, thereby removing the *locus minoris resistentiae* and making it possible for the affected tissues to overcome the infection.

The treatment practically prevents embolism.

The treatment must be supplemented by the removal of primary foci in the oral cavity and secondary foci in the jugular veins to prevent reinfection of the veins of the leg.

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## MULTIPLE RETROGRADE SAPHENOUS VEIN LIGATION AND PHLEBECTOMY WITH AID OF MALLEABLE INTRALUMINAL GUIDE

ARKELL M. VARGIN, M.D., CHICAGO, ILL.

(From the Department of Surgery, Loyola University School of Medicine and Mercy Hospital)

HIGH saphenous vein ligation combined with multiple retrograde ligations and excision of segments of the vein is superior, in my experience, to high ligation plus retrograde injection of a sclerosing solution.

In this procedure locating the saphenous vein above the knee is often difficult, especially in obese patients. To overcome this difficulty a malleable intraluminal guide, such as a flexible medium sized uterine probe, is inserted into the lumen of the vein near the fossae ovalis area and passed downward. The vein is easily located over the probe above the knee and can be readily dissected out. This procedure can be repeated down the course of the vein above and below the knee. This maneuver has aided in vein operations and it is presented here to other surgeons for their evaluation.

For several years, high ligation was combined with retrograde injection of a sclerosing solution. It was observed that patients who received retrograde injections were, for the first few days, more uncomfortable and disabled than were those who had ligation only. This was due to a chemical phlebitis which in some instances was quite severe. It was observed further that many patients who consulted me two or more years after operation elsewhere with retrograde injection had large recurrent varicosities either above or below the knee or both. Many times re-operation revealed that recurrence was due to inadequate surgery at the first operation. Large incompetent external or internal femoral cutaneous veins arising near the fossae ovalis were found. These had not been ligated previously and subsequently dilated. In some instances the saphenous had been entirely overlooked, but a rather large external or internal femoral cutaneous ligated, in the belief that the saphenous vein was being ligated. The reason for recurrence in these cases was obvious.

Another group of patients observed were those who had been operated upon previously with meticulous care. All the branches entering the saphenous at the fossae ovalis had been ligated and four to six inches of the vein had been resected distally. Up to 10 c.c. of a sclerosing solution had been injected into the distal part of the vein. Many of these patients returned in two years or more with recurrences below the knee and occasionally both above and below the knee. The recurrence in these cases was not due to inadequate previous surgery but, in my opinion, to incompetent communicating veins or recanalization of the thrombi following the retrograde injection or possibly a combination of both.

Still another group of patients were those who presented themselves with recurrences, who had previous ligation and injection elsewhere by competent

surgeons in recognized clinics and hospitals. Recently one of these patients who had been operated upon four years before, with recurrence, was re-operated upon. The fossae ovalis area was re-explored and nothing found except a fibrous cord which represented the previous ligated and injected saphenous vein. This fibrosed vein extended about six inches below the fossae ovalis and then began to dilate and presented a varicose vein both above and below the knee. A cross section of the vein in the thigh (Fig. 1) above (Fig. 2) and below the knee (Fig. 3) revealed that in the thigh the vein was almost completely fibrosed, there being a very small lumen in its center (Fig. 1). Above the knee one side of the vein showed evidence of previous thrombosis which was organized, but was greatly dilated (Fig. 2). Below the knee the vein was greatly dilated with evidence of previous thrombosis (Fig. 3). The recurrence in these cases above or below the knee was not due to inadequate surgery, but in my opinion to a recanalization of the thrombus, possibly aided by incompetent communicating and perforating veins.

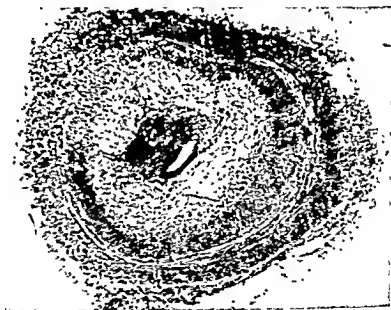


Fig. 1.—Cross section of saphenous vein in the upper thigh about four inches below fossae ovalis. A thorough ligation with retrograde injection was performed four years previously. Note the organization of old thrombus and canalization.

From these observations it was concluded that recurrences above and below the knee were not always due to inadequate surgery or collateral proliferation, but to a recanalization of the thrombosed vein which was possibly aided by an incompetent communicating or perforating vein down the course of the vein.

Consequently, it was decided to attempt retrograde ligation with excision of segments of the vein both above and below the knee along with high saphenous ligation rather than retrograde injection. This I have been doing for the past five years.



Fig. 2—Cross section of same vein just above the knee. Note the marked eccentric thickening of vein wall due to organization of pre-existing thrombus.



Fig. 3—Cross section of same saphenous vein below the knee. Note the evidence of previous sclerosis with organization and almost complete restoration of patency of vein. This has occurred in the past four years.



The saphenous vein, many times, is more difficult to locate above the knee than in the femoral triangle (Scarpa) (Fig. 4, A), especially in obese individuals. To overcome this difficulty the idea was conceived of inserting a malleable intraluminal guide into the distal segment of the vein near the fossae ovalis (Fig. 4, C). A ligature is placed around the distal end and held tight to prevent the reflux of blood while the guide is being inserted (Fig. 4, C). The

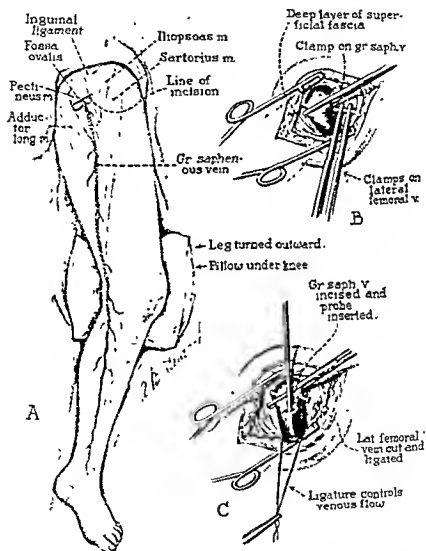


Fig. 4.—Diagram showing (A) location of fossae ovalis in apex of femoral triangle and course of saphenous vein down the leg. (B) Lateral femoral cutaneous vein being clamped. (C) malleable intraluminal guide being inserted into vein near fossae ovalis.

guide follows the lumen of the vein and can easily be palpated through the subcutaneous tissue. An incision is made over the guide in mid-thigh and the vein easily exposed and dissected out (Fig 5, *A* and *B*). The proximal end is doubly ligated (Fig. 5, *C* and *D*), a segment removed, and the guide withdrawn. The distal end is clamped with a hemostat since the guide will be inserted into the distal end later (Fig. 8, *A*)

Second incision.

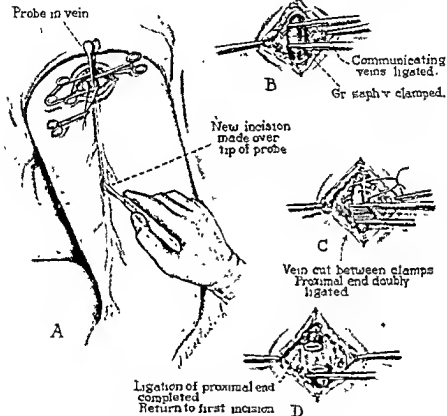


Fig 5.—Diagram showing (*A*) an incision being made in mid-thigh over the guide (*B*) vein dissected out and communicating vein, dissected and ligated (*C*) and (*D*) double ligation of proximal end of vein

Many times a communicating vein (Fig 5, *B*) is isolated and ligated. An aneurysm may be found opposite the entrance of an incompetent communicating vein (Fig. 7). Sometimes the guide enters one of these aneurysms or a communicating vein (Fig 7). This aids in locating a communicating vein. When the communicating vein is dissected out, the guide can be pulled out a short distance and reinserted into the lumen of the saphenous after the communicating vein or aneurysm has been isolated.

The guide is withdrawn after the proximal ligation in mid-thigh has been completed. The distal end of the saphenous in the femoral triangle is doubly ligated, one ligature being transfixed (Fig. 6, A). Cotton, No. 30 for the larger veins and No. 40 for the smaller vessels, is used throughout the operation, except for the skin where interrupted dermal is used.

The lateral femoral cutaneous (Fig. 4, B and C) and medial femoral cutaneous veins if present may be ligated and cut at this time if this was not done previous to inserting the intraluminal guide. Likewise the superficial external

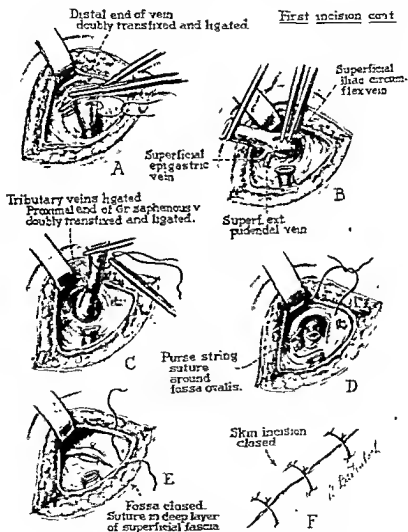


Fig. 6.—Diagram showing fossae ovalis and branches usually found in this area.

pubdental vein or veins, since usually there are more than one (Fig. 6, *B*), the superficial circumflex iliac (Fig. 6, *B*), and the superficial epigastric (Fig. 6, *B*) are ligated and cut.

The saphenous vein is dissected at the fossae ovalis down to its entrance into the femoral. This dissection as well as all blood vessel dissections is facilitated by using a small piece of umbilical tape rolled up and clamped to the end of a hemostat (Fig. 9). It is then doubly ligated snug to the femoral vein, one ligature being transfixed and the segment of vein cut and removed (Fig. 6, *C*).

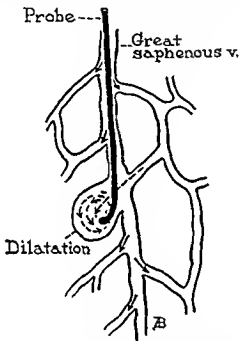


Fig. 7.—Diagram showing how guide may locate an aneurysm or communicating vein.

The fossae ovalis is closed with a purse-string suture (Fig. 6, *D*). The deep layer of the superficial fascia is approximated (Fig. 6, *E*) and the skin closed with interrupted dermal (Fig. 6, *F*).

Next a return is made to the mid-thigh incision (Fig. 8). The intraluminal guide is again inserted into the distal end of the vein, palpated above the knee, and the vein easily located, exposed, dissected out, and a segment removed and ligated (Fig. 8, *A*). Again the guide is withdrawn and the distal end of the vein in the mid-thigh incision ligated. The proximal end of the vein at the knee incision is ligated, but the distal end clamped as before.

The guide is next inserted down the vein from the knee incision to below the knee where the vein is again palpated over the guide, exposed, dissected out, ligated, and resected as before. This can be repeated to near the termination of the saphenous vein (Fig. 8, *B*).

The dilated veins seen below the knee when standing usually prove to be branches of the main vein. The guide may enter this superficial communication but can be withdrawn a short distance, manipulated, and then enter the main vein which arises near the medial malleolus. This has been demonstrated numerous times.

Second incision cont.

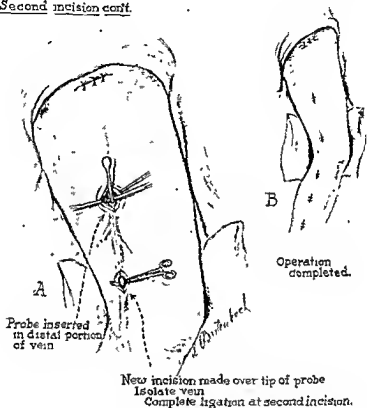


Fig 8—Diagram showing (A) the guide being inserted at the mid-thigh incision into the distal end of the vein. The vein is again isolated just above the knee with the aid of the intraluminal guide. (B) Showing end result of retrograde ligation and phlebectomy above and below the knee.

The malleable intraluminal guide may be used further by exposing and opening the saphenous vein above or below the knee and directing it upward. This maneuver aids in determining whether the saphenous was properly ligated previously at the fossae ovalis. If not, a religation and excision are indicated. It further aids in determining the extent, if any, of the sclerosis.

Longitudinal incisions, in my experience, heal better than transverse ones and give a better cosmetic result. So far none of the patients have complained of the resulting scar, which in most instances is minimal and hardly visible after a few years.

An elastic adhesive bandage or Unna's boot, if a varicose ulcer is present, is applied from the toes to the knee. The patient is ambulatory two hours after operation. The stitches are removed in one week. The incisions usually heal by first intention and infection is rare.

Recurrences may and do occur with this procedure but in my experience not as frequently as when retrograde injection is used. If recurrences do occur it is by the formation of new collaterals rather than by organization of a thrombus alone. A thrombus will organize more quickly and frequently than collaterals will form. If recurrences do occur they can be treated by injection of the collaterals when they appear or by further ligation.

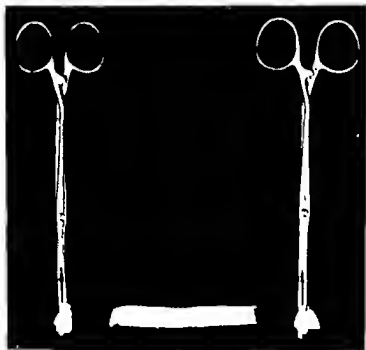


Fig 9—Photograph showing piece of umbilical tape rolled up and attached to the end of a hemostat. This provides dry gauze dissection without bulk which is encountered when large dry sponges are used. This aids in dissection of veins.

McPheeters\* has wisely stated that patients who are prone to develop varicose veins should consult their physician at regular intervals for inspection and injection of any new varicosities, just as they should visit their dentist for inspection and care of their teeth.

This procedure is presented not as a cure-all for varicose veins, but as a method of procedure which has helped in the surgical treatment of varicose veins. The procedure is thought to be surgically sound and it is hoped that others may profit by this report.

\*McPheeters, 11 O : Surg. Gynec. & Obst. 41 353-364 1945

## STIMULANT

1. Various tubes may occur following skin eruptions located confined with restricted margins. This condition may follow immediate surgery in the genital triangle resulting in a severe flow of blood upon the skin, which in turn may become restricted.

2. Various tubes may occur following abdominal surgery in the genital triangle confined with restricted margins. This condition may be due to interrupted communication or perforating tube which causes restriction of the circulation in the triangle.

3. A contracted tube has a tendency to restrict flow.

4. Restricted tubes a and b and c and d of segments of the apparatus with a different length above and below the knee should illustrate any severe flow of blood which in the same form interrupted communication or perforating tube exists up.

5. Restricted tubes a and b and c in my opinion are subject to restricted system.

6. A contracted maladaptive functional tube facilitates during the apparatus with both above and below the knee, and many times is located in interrupted communication or perforating tube or segment.

7. Cotton is a good secure material as there is little or no tissue reaction following its use.

8. A small piece of tubular type rubber type held and attached to a bandage facilitates diversion of the tube.

9. Localized lesions are subject to transient lesions in restricted apparatus motion and physiology.

## GRADED LEG EXERCISES

JOSEPH K. NARAT, M.D., AND ARTHUR F. CIPOLLA, M.D., CHICAGO, ILL.

UNTIL the problem of a successful therapy of pulmonary embolism has been solved, all efforts must be concentrated on its prevention.

Collins<sup>1</sup> tabulated the incidence of pulmonary embolism as reported in the literature during the preceding twenty-four years by fifteen authors. In 316,060 cases the incidence was determined to be 0.52 per cent. In 172,888 operations of all types performed at the Mayo Clinic<sup>2</sup> there were 343 fatal emboli, indicating an incidence of 0.2 per cent of 1 in 500 cases. Pulmonary embolism accounted for 5.9 per cent of all postoperative deaths. A survey of large collective statistics by de Takats and Jesser<sup>3</sup> revealed a fairly steady incidence in large services, namely, from 0.1 to 0.2 per cent of all operations, 2 per cent of all deaths, and 6 per cent of postoperative deaths. Erskine and Shires<sup>4</sup> found that the mortality from pulmonary embolism after abdominal operations performed at the Chelsea Hospital for Women was 0.415 per cent or 1 fatal embolism in 240.5 operations.

The frequency of pulmonary embolism in obstetrics is similar to that following surgery. Nettleblad<sup>5</sup> reported 0.86 per cent of thrombosis and embolism in 50,000 deliveries.

It can be seen from the previously mentioned statistical data that the incidence of postoperative or post-partum pulmonary embolism is too small to warrant the routine employment of prophylactic measures. This applies especially to those which require supervision of the nursing personnel and thus consume their valuable time. On the other hand, no effort should be spared to prevent occurrence of this tragedy in cases where such a complication may be expected. Patients with hypotension, cardiac diseases, varicosities of lower extremities, abdominal distention, obese individuals, patients over 50 years of age, those with a past history of a peripheral vascular disease or blood dyscrasia as well as those who are convalescing from an extensive or technically difficult pelvic laparotomy are prospective victims of a venous thromboembolic disease. It is in this group of patients that the following prophylactic measures are in order: (1) leg exercises to prevent stagnation of the blood column, (2) no tight binders which form a mechanical obstruction to the venous backflow, (3) Trendelenburg position to facilitate the return of venous blood from the lower extremities by the effect of gravity,<sup>3,6</sup> (4) avoidance of Fowler's position which causes stasis in the lower legs because of their pendancy and the compression or kinking of the popliteal veins,<sup>7</sup> (5) encouragement of deep respirations essential for propulsion of blood, (6) early ambulation, (7) early administration of fluids to counteract dehydration with resulting hemoconcentration, (8) dietary regime<sup>8</sup> (low fat, low protein diet as the least conducive to thrombotic changes), (9) frequent change of position, (10) employment of dicumarol or heparin in selected cases.



The discussion of all these and other measures is beyond the scope of this paper. There is a general agreement that two measures deserve the greatest attention in the prophylaxis of pulmonary embolism: (1) leg exercises and (2) use of heparin and dicumarol in selected cases.

Stagnation of venous blood is one of the most readily controllable factors in postoperative thrombosis. In view of the fact that the most common source of thrombosis leading to embolism is the femoral vein and its tributaries, the lower extremities are receiving the greatest attention in attempts to maintain the muscle tone and to promote the flow of venous blood. For this purpose Pool<sup>7</sup> suggested a set of active exercises and early ambulation. Various devices have been developed for active and passive exercises; rollers against which the patient is instructed to rub his feet and legs,<sup>11</sup> rhythmically contracting air cushions strapped to the patient's legs,<sup>12</sup> levers raising and lowering the patient's limbs,<sup>13</sup> pedaling apparatus,<sup>14</sup> "a device consisting of a stand which carries two pulleys with counterbalance weights,"<sup>15</sup> oscillating bed,<sup>16</sup> an apparatus operated by patient's hands.<sup>17</sup>

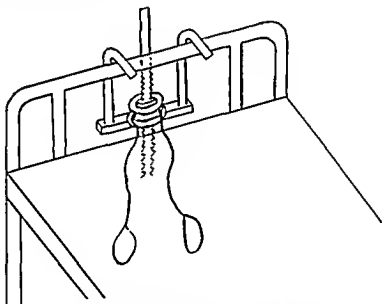


FIG. 1—Leg exerciser mounted on the foot of the bed.

The efficiency of postoperative exercises in prevention of pulmonary embolism is attested by Erskine and Shires<sup>4</sup> who reported that the incidence of fatal embolism after abdominal operations was reduced by more than one-half following introduction of postoperative exercises and massage. Shaw and Rickards<sup>18</sup> found fatal embolism to be five times more common in a hospital where exercises are not included in the postoperative treatment as compared with another institution where exercises are carried out as a routine.

While the value of leg exercises has thus been established, certain disadvantages of the devices now in use must be mentioned: most of them are bulky

and either take considerable space in the bed, interfering with the patient's comfort, or protrude from the bed, blocking the free passage in the room; patients must be uncovered to perform the exercises, some devices are impractical or expensive or both; they are time consuming because they require supervision; finally, they provide no facilities for registration which is essential because pain, lack of interest, or lassitude caused by sedation may prevent the patient from faithfully carrying out the prescribed order.

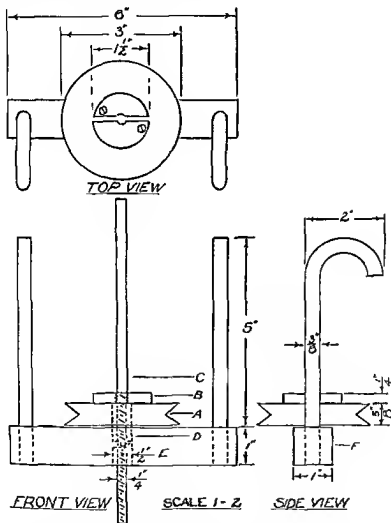


Fig. 2—Mechanical drawing of leg exerciser.

To overcome such shortcomings, we developed a leg exerciser<sup>11</sup> which is relatively low in cost, has a simple construction, requires very little space, does not require uncovering the patient, and registers the number of exercises. The apparatus consists essentially of a pulley which rotates whenever a cord placed

around it is pulled by the patient's feet. A vertical rod attached to the pulley trips the arm of a counting machine. This device saves valuable time of the nursing personnel because no supervision is required; a glance at the counting chamber shows whether the patient carried out the exercises as directed.

In an attempt to simplify the device further and to make it still less expensive and more sturdy, we developed a new apparatus for calisthenic exercises of lower extremities.

The main parts of the apparatus are a pulley and a vertical threaded rod mounted on a crossbar and attached to the foot of the bed with two hooks. The pulley is equipped with a cord whose ends are attached to the patient's feet or ankles. When the patient alternately flexes his knees, the pulley rotates, causing the vertical shaft to rise. As the rod is marked with numerals, it is easy to check whether the patient performed the number of exercises prescribed.

#### TECHNICAL DETAILS

A pulley (A) 3 inches in diameter with a  $\frac{1}{2}$  inch hole carries a disk (B)  $\frac{1}{4}$  inch thick and  $\frac{1}{2}$  inch in diameter. The disk is tapped with a No 14-28 S. A. E. thread and is split in the vertical plane. The disk is attached to the top of the pulley with two screws. A 14-28 S. A. E. threaded rod (C) rides the center of the threaded disk. The rod is ground  $\frac{1}{16}$  inch on one side throughout its entire length. The center of the pulley is equipped with a bushing (D)  $\frac{1}{2}$  inch in diameter, with a  $\frac{1}{4}$  inch central hole; at the bottom end of the upper bushing there are two  $\frac{1}{8}$  by  $\frac{1}{8}$  inch prongs which fit a lower bushing (E) containing two spiral grooves to fit the prongs in the form of a ratchet. This ratchet allows the upper bushing to move in one direction only. The upper bushing is fixed to the pulley while the lower is attached to the cross-bar (F) 1 by 1 by 6 inches. The lower bushing contains a hole through which an S-32 standard screw is inserted. This screw rides the ground surface of the vertical rod.

#### SUMMARY

A new apparatus for leg exercises has a very simple construction, is inexpensive, occupies practically no space, does not require uncovering the patient, and registers the number of exercises.

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## SUCCESSFUL PRIMARY REPAIR OF LACERATED STENSON'S DUCT

RALPH E. GOODALL, M.D., AND SARAH E. FLANDERS, M.D., NEW YORK, N. Y.

(From the Second [Cornell] Surgical Division of Bellevue Hospital)

THE anatomic location of Stenson's duct makes it subject to injury in deep wounds of the cheek. As failure to repair the duct results in a salivary fistula with its distressing symptoms, it is imperative to attempt to reapproximate the divided ends at the time of initial débridement. Eight cases of primary suture of Stenson's duct have been recorded in the literature and the method used varied but slightly in each instance. Success of the procedure seems to have depended on the use of an inlying dowel firmly fixed in place at the time of early débridement and on the anatomic structure of the duct which makes it suitable for suture. It is our purpose, after a brief review of the anatomy, to report another case of primary suture of the parotid duct and to show the success of the procedure by accompanying pictures of the patient and sialograms taken six months following operation.

### ANATOMY

The parotid duct measures two and one-half inches in length. Its surface anatomy corresponds to a line drawn across the face about one fingerbreadth below the zygoma running from the tragus to a point midway between the vermilion border of the upper lip and the ala of the nose. In its course it crosses over the masseter muscle at the anterior border of which it dips down into the substance of the upper part of the buccinator muscle, which it pierces, and then runs obliquely forward for a short distance between the buccinator muscle and the oral mucous membrane. The opening on the inner surface of the cheek is through an orifice opposite the second upper molar tooth. The wall of the duct is dense and of considerable thickness, consisting of an external fibrous coat containing contractile muscle fibers and an internal mucous coat lined with short columnar epithelium.

### CASE REPORT

E. M., a 35 year old white man, was admitted to Bellevue Hospital on Dec 31, 1914, with multiple lacerations of the face and hands, having been assaulted with a sharp instrument about one hour prior to admission. On physical examination the patient was conscious but with a strongly alcoholic odor to the breath. There was a deep laceration, 6 cm. in length, extending obliquely from over the zygoma at a point about 3 cm. anterior to the tragus of the left ear almost to the midpoint of the body of the mandible. The buccal mucosa was intact. He was unable to move the left side of the face. There was also a 2 cm. laceration just over the lateral margin of the left eyebrow and a 2 cm. laceration at the base of the nose extending just above the left eyebrow. A 6 cm. laceration extended across the knuckles of the third to the fifth fingers of the left hand with division of the tendons where the assaulting instrument had penetrated directly into the bony substance partly severing the metacarpal heads. He had a flexion deformity of the third to the fifth fingers due to a pre-existing Dupuytren's contracture. A similar deformity involved the fifth

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finger of the right hand and there was a superficial laceration of the right thumb. The rest of the physical examination was within normal limits except for an old upper right rectus scar.

Two hours after admission a débridement and suture of the multiple lacerations were performed under sodium pentothal anesthesia. All wounds were uncomplicated except for the one in front of the left ear where exploration revealed complete division of Stenson's duct in the masseteric portion and division of three terminal branchia of the facial nerve. The wound was cleansed with green soap and peroxide and irrigated with approximately 6 L. of physiologic saline solution over a period of twenty minutes. All devitalized tissue was removed. The masseter muscle was sutured with 000 plain catgut. An attempt was made to approximate the severed ends of the facial nerve branchia but the small caliber of the nerves made accurate approximation doubtful. The proximal end of the severed



Fig. 1

Fig. 2

Fig. 3.

Fig. 1—Healed laceration at six months.

Fig. 2—Facial paralysis resulting from division of branches of facial nerve.

Fig. 3—Facial paralysis.

duct was easily identified. The distal end was located by passing a small ureteral catheter through the orifice in the mouth. When the catheter emerged in the laceration, it was passed into the proximal segment of the duct. The two ends were then sutured over the catheter, using interrupted sutures of fine black silk. Primary closure of the wound was effected by approximation of subcutaneous tissues with interrupted sutures of 000 plain catgut and of the skin edges with vertical mattress sutures of black silk. The catheter was taped securely to the lower lip to hold it in place, and a dry sterile dressing was applied. A tenorrhaphy was performed on the left hand.

Postoperatively the patient was given nothing by mouth, and oral hygiene was maintained by mouth care every two hours. He had a slight temperature elevation for four days, spiking to 103° F. on the fifth and sixth days, with subsequent return to normal. On the fourth postoperative day there was slight swelling over the left parotid gland. The wound, however, was clean and the skin silks were removed. There was slight reaction about the orifice of the duct in the mouth. No flow of saliva was noted. The catheter was removed on the fifth postoperative day. The patient was fed parenterally until the sixth day when he was placed on a full fluid diet. Change to a soft diet on the seventh postoperative day was tolerated well by the patient, with no swelling or pain in the region of the left parotid gland, and a free flow of saliva was noted from the stoma of Stenson's duct. Be-

cause of the left facial paralysis, the eye department performed a tarsorrhaphy on the twelfth postoperative day. This was unsuccessful. He was discharged from the hospital on the eighteenth postoperative day. He was contacted six months later, at which time the pictures (Figs 1, 2, and 3) and the sialograms (Figs. 4 and 5) were taken. There was no fistula, no swelling, and no tenderness of the parotid gland, and the sialograms showed a normal pattern with no stenosis of the duct.

Fig. 4.

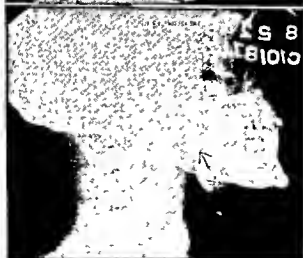
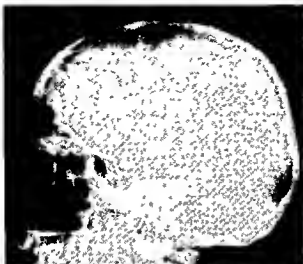


Fig 5.

Fig. 4.—Sialogram six months postoperative

Fig 5.—Sialogram six months postoperative

#### DISCUSSION

Even though the reported cases show a variance in the form of treatment, certain constant factors are found: Débridement and suture were carried out



passed through the duct as an inlying dowel, and silk was used to approximate the ends of the duct. Fixation of the dowel in place was accomplished by tapping to the lower lip. The patient had a satisfactory postoperative course. When seen six months later he had no symptoms referable to the parotid gland and a sialogram showed no abnormalities of the duct.

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## THE USE OF PENICILLIN IN CONNECTION WITH THE GRAFTING OF BONE INTO INFECTED DEFECTS IN THE SKULLS OF EXPERIMENTAL ANIMALS

H. J. MCCORKLE, M.D., EDWIN KERR, M.D., SANFORD ROTHFENBERG, M.D., AND  
HELEN WARNER, A.B., SAN FRANCISCO, CALIF.

(From the Division of Experimental Surgery of the University of California Medical School)

INFECTED bone defects were produced in the skulls of dogs by excising segments of bone, crushing the temporal muscles, contaminating the wounds with street dirt, and closing them with sutures (Fig. 1). After the acute phase of the infections subsided, chronic granulating wounds and sinuses remained. A considerable number of trial experiments were performed before suitable uniform chronic infected skull defects were produced by this method. Twenty dogs with well-established infections were selected for the main experiments. Bacteriologic cultures were made from the wounds and from the infected tissues removed surgically, and penicillin-sensitivity studies were carried out. In Table I are listed the bacteria cultured from the infected wounds of the twenty animals before the bone grafting procedures.

After the chronic infections had become well established, the animals were subjected to operations, at which granulations, sear, and sequestra were removed, bone grafts placed in the skull defects (and retained in position with fine steel wires placed through small drill holes), and the wounds closed in layers with cotton sutures without drainage (Fig. 2). In one-half of the animals cortical bone grafts were used, and in the others cancellous bone was used for the grafts. Ten animals (five cortical grafts and five cancellous grafts) were used as controls, and the other ten (five cortical and five cancellous grafts) were given 100,000 units of penicillin daily for two days preoperatively and for twenty-one days postoperatively. Penicillin was given by intramuscular injection at four-hour intervals.

The soft tissue wounds of eight of the ten animals treated with penicillin healed without infection. Trivial infections appeared in two of the penicillin-treated animals, one of these developed a hematoma infected with *P. vulgaris*; the other healed per primam, but five weeks postoperatively developed a small draining sinus, from which penicillin-sensitive organisms were cultured (this healed with additional penicillin therapy). The wounds of nine of the ten untreated control animals broke down with acute gross infection within the first few postoperative days; the remaining control animal developed multiple suture hole abscesses and slight drainage from the anterior aspect of the incision. Signs of illness from general sepsis were obviously present in all untreated control animals, they appeared thin and lethargic, and ate poorly. All

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of the ten penicillin-treated animals were entirely free of signs of toxicity from sepsis, were alert and active, and had good appetites. In Table II are summarized the manifestations of infection in these twenty experimental animals.

One of the penicillin-treated animals died thirty nine days postoperatively, from causes beyond the control of the experimenters, but the other nine survived with well-healed wounds for the remainder of the six-month postoperative experimental period. In the control group the wounds of two of the animals suppurated for one to two months postoperatively, those of seven animals sup-



Fig. 1.—Diagrams indicating method for producing experimental infected skull defects in animals

TABLE I

ORGANISM	NUMBER OF ANIMALS	PENICILLIN SENSITIVE	PENICILLIN RESISTANT
Beta hemolytic Streptococcus	14	13	1
Alpha hemolytic Streptococcus	2	1	1
Gamma Streptococcus	9	1	8
Hemolytic Staphylococcus aureus	11	11	0
Hemolytic Staphylococcus albus	8	8	0
Nonhemolytic Staphylococcus aureus	3	3	0
Nonhemolytic Staphylococcus albus	3	2	1
Clostridia	18	18	0
Escherichia coli	8	0	8
Aerobacter aerogenes	3	0	3
Bacillus pyocyaneus	1	0	1
Proteus vulgaris	2	0	2
Diphtheroid bacilli	7	0	7
Bacteroides	2	—	—

TABLE II

	ILLNESS FROM SEPSIS	HEALING OF SOFT TISSUE WOUNDS		
		WITHOUT INFECTION	TRIVIAL INFECTION	GROSS INFECTION
Penicillin treated	0	8	2	0
Controls	10	0	1	9

purated for two to three months after operation, and the wound of one animal suppurated for the entire six-month postoperative experimental period.

X-ray examinations of the bone-grafted areas were made at appropriate intervals during the postoperative period. The x-ray views in the group of animals treated with penicillin in the early postoperative period revealed sharply outlined grafts that remained unchanged in size or position, and without evidence of absorption of the grafted bone (except for one small area near a drill hole in one graft, which probably was caused by compression due to a tight wire). X-ray evidence of bony union between the graft and the skull appeared between the fifth and twentieth postoperative weeks in eight of the nine penicillin-treated animals. The x-ray evidence of bone repair did not differ significantly

TABLE III

	NUMBER OF ANIMALS	X-RAY APPEARANCE OF BONE GRAFT				
		AFFAIENTLY VISIBLE	ABSORBED	COMPLETE SEQUESTRATION	EXTRUSION	BONY UNION
Penicillin treated	9	9	0	0	0	8
Controls	10	2	5	1	2	2

TABLE IV

	NUMBER OF ANIMALS	VIABLE GRAFTS	EXTENSION—SCAR REPLACEMENT	ABSORPTION—REPLACEMENT WITH SCAR	SEQUESTRATION OF GRAFT	BONY UNION
Penicillin treated	9	9	0	0	0	8
Controls	10	2	2	5*	1	2

\*In two of these animals very small residual pieces of the original bone grafts were imbedded in extensive scar.

in the cortical and cancellous grafts. The x ray studies in the untreated control animals indicated evidence of decrease in size and extensive absorption of the grafts in eight out of ten animals. In these eight animals, five of the grafts were partially or completely absorbed, two were extruded through the open infected wounds, and one remained in place without attachment, as a sequestrum. In the other two control animals, one had x ray evidence of apparent viability and bony union between graft and skull, the other had x ray evidence of decreased size and density from absorption, but later regained its normal density and also developed x ray signs of bony union between two sides of the graft and the skull defect. In Table III are summarized the x ray findings in this group of nine penicillin treated and ten control animals.

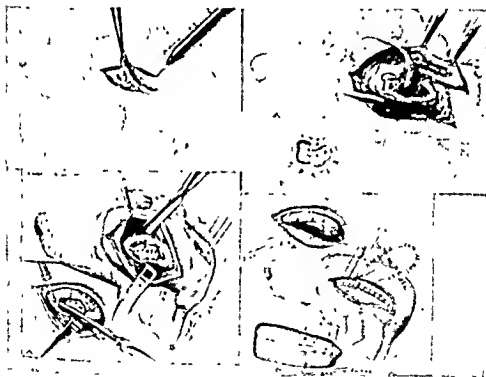


Fig. 2.—Diagram illustrating method for removal of infected tissues and placing grafts into the skull defects (aseptic surgical technique was used).

The nineteen experimental animals (nine penicillin-treated and ten untreated control animals) were sacrificed six months after the bone grafting operations. In nine penicillin-treated animals full-sized healthy viable bone grafts were found in all cases, although in one graft a very small area beneath a wire had been absorbed, confirming the x-ray findings in the same animal. Bony union between the grafts and the margins of the skull defects was present in eight of the nine penicillin-treated animals. In five of the animals this union was present on all four sides, in one animal union had occurred on three sides,

TABLE I

ORGANISM	NUMBER OF ANIMALS	PENICILLIN SENSITIVE	PENICILLIN RESISTANT
Beta hemolytic <i>Streptococcus</i>	14	13	1
Alpha hemolytic <i>Streptococcus</i>	2	1	1
Gamma <i>Streptococcus</i>	9	1	8
Hemolytic <i>Staphylococcus aureus</i>	11	11	0
Hemolytic <i>Staphylococcus albus</i>	8	8	0
Nonhemolytic <i>Staphylococcus aureus</i>	3	3	0
Nonhemolytic <i>Staphylococcus albus</i>	3	2	1
<i>Clostridia</i>	18	18	0
<i>Escherichia coli</i>	8	0	8
<i>Aerobacter aerogenes</i>	3	0	3
<i>Bacillus pyocyaneus</i>	1	0	1
<i>Proteus vulgaris</i>	2	0	2
Diphtheroid bacilli	7	0	7
Bacteroides	2	—	—

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X-ray examinations of the bone-grafted areas were made at appropriate intervals during the postoperative period. The x-ray views in the group of animals treated with penicillin in the early postoperative period revealed sharply outlined grafts that remained unchanged in size or position, and without evidence of absorption of the grafted bone (except for one small area near a drill hole in one graft, which probably was caused by compression due to a tight wire). X-ray evidence of bony union between the graft and the skull appeared between the fifth and twentieth postoperative weeks in eight of the nine penicillin-treated animals. The x-ray evidence of bone repair did not differ significantly

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		APPARENTLY VIABLE	ABSORBED	COMPLETE SEQUESTRATION	EXTRUSION	BONY UNION
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Controls	10	2	5	1	2	2

TABLE IV

	NUMBER OF ANIMALS	VIABLE GRAFTS	EXTRUSION—SCAR REPLACEMENT	ABSORPTION—REPLACEMENT WITH SCAR	SEQUESTRATION OF GRAFT	BONY UNION
Penicillin treated	9	9	0	0	0	8
Controls	10	2	2	5*	1	2

\*In two of these animals very small residual pieces of the original bone grafts were imbedded in extensive scar.

## NEUROFIBROMA OF THE POSTERIOR MEDIASTINUM

I. DAVIS PUTTEL, M.D., COLUMBUS, OHIO

(From the Department of Research Surgery of the Ohio State University)

**I**NRATHORACIC tumors of neurogenic origin are rare, records of 141 cases having been found by me in the literature. There is no doubt that many more exist than have been reported heretofore, as evidenced by the character of the cases collected from various Army Thoracic Surgery Centers in the United States and reported by Blades.<sup>1</sup> Routine roentgenographic examination of the chest led to the detection of more than 85 per cent of the mediastinal tumors in his series. These in many instances presented no clinical manifestations. Of 109 patients who were operated upon for mediastinal tumors over a period of about three years, 29 cases showed benign types of neurogenic origin and each patient was treated successfully by surgical extirpation of the tumor.

Graham and his associates<sup>2</sup> called attention to the real danger of these mediastinal tumors so that now it is generally accepted that benign tumors of neurogenic origin, even though asymptomatic, should be removed to prevent malignant change which so often occurs in the untreated patients. After malignant transformation has appeared, the prognosis often is hopeless and surgical intervention frequently proves curatively ineffective.

At the present time, excision is relatively simple in the usual case of benign tumor and the mortality rate is minimal provided the refined principles of thoracic surgery, of pre- and postoperative care, and of anesthesia are followed. This procedure can be carried out easily even by a general surgeon under proper conditions, provided he applies the principles of modern thoracic surgery.

It has again been emphasized in my patient, as has so often occurred, that roentgenotherapy, which was given elsewhere, proved futile in an attempt to treat the tumor.

### CASE REPORT

P. C. (Hosp. No. 453981), a white laborer 61 years of age, was admitted to University Hospital, June 25, 1945. He had minimal symptoms in the chest consisting of mild intermittent dyspnea and an occasional choking sensation particularly when in bed and lying on the right side. Four years prior to admission he was believed to have had heart disease. At that time electrocardiography and roentgenography of the chest were made elsewhere. These revealed what the cardiologist believed to be evidences of coronary heart disease as well as an intrathoracic tumor. The patient was then told that surgical intervention would be dangerous and radiation therapy alone could be considered in treatment of the tumor. Consequently, from July 17 to Aug. 2, 1941, the patient was given over the tumor anteriorly and posteriorly a total of 4,290 roentgen units in sixteen divided daily doses following the technique of Coutard. The tumor proved to be radioresistant and therapy was abandoned. The patient visited several physicians in the next four years who treated him expectantly and without improvement. He became generally nervous, suffered insomnia, and lost about twenty pounds in body weight, principally due to worry about the tumor and his future.

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C.

B.

A.

Fig. 1.—Anteroposterior and lateral x-ray views of the thorax show the typical position and shape of a primary benign tumor of the posterior mediastinum (B and C) in 1946 and practically no change in its size when compared to a roentgenogram (A) taken in 1941.

I saw him first in June, 1945, at which time a roentgenogram (Fig. 1, B) revealed no appreciable change in the size or shape of the tumor when compared to the roentgenogram (Fig. 1, A) which was obtained in 1941, prior to the course of x ray therapy. I advised that he be hospitalized. The rest of the history was not remarkable.

Physical examination disclosed a well nourished and well developed white man who was in apparent good health. The thorax was symmetrical and its expansions equal. The lungs were clear to percussion and auscultation. Breath sounds were normal throughout and there were no rales. The heart was not enlarged, its sounds were of good quality, and there were no murmurs present. The remainder of the examination was also negative.



Fig 2—This radiogram at six months following operation reveals no abnormalities except for missing segments of the sixth, seventh and eighth ribs

On admission the red blood count was 4,310,000, with the hemoglobin 13.2 Gm. per cent. The white blood count was 5,200, with the neutrophils 63 per cent, lymphocytes 21 per cent, monocytes 7 per cent, and eosinophils 9 per cent. The urinalysis was negative. The blood Mazzini and Kahn reactions for syphilis were negative. The blood urea nitrogen was 15.5 mg. per cent, which is normal. Phenolsulfonphthalein intravenously showed 40 per cent excretion during the first hour and 20 per cent during the second hour, which are normal. An electrocardiogram revealed left axis deviation, slurring of the QRS complexes, deep Q<sub>4</sub> waves, prolonged ventricular conduction, abnormal ST intervals, and abnormal T waves, which are indicative of myocardial damage with a ventricular conduction defect. Skiagrams of the chest (Fig. 1) showed a sharply circumscribed spherical mass located far posteriorly in the right mediastinum. It extended from the level of the sixth to the ninth ribs posteriorly. It extended anteriorly to just back of the bifurcation of the trachea (Fig. 1, C). Radiographs of the spine and ribs were taken, but revealed no gross changes. There were no cord symptoms to suggest a dumbbell type of tumor.

A diagnosis of probable primary benign tumor of neurogenic origin was made and the patient was advised that excision be performed in order to preclude and prevent malignant degeneration. One gram of sulfadiazine and 0.6 Gm. of sodium bicarbonate were administered four times daily beginning June 25. Penicillin was given intramuscularly in doses





Fig. 3.—The tumor as removed weighed 60 Gm., it was spherical and well encapsulated. The portions of ribs removed are shown.

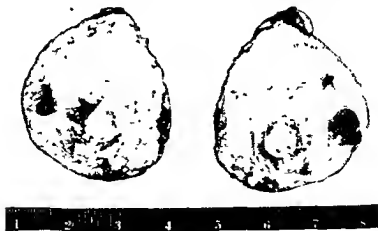


Fig. 4.—Cross section revealed a variegated appearance showing areas of old hemorrhage, cyst formation, and yellow tissue in a background of firm grayish tissue.

of 12,500 units every three hours beginning June 27. Adequate amounts of vitamins C and K were furnished.

Under pentothal sodium intravenously for induction and endotracheal anesthesia using cyclopropane, ether, oxygen, and helium, I performed the operation on June 28, using the usual posterolateral approach through the bed of the seventh rib. From the transverse processes outward, 13 cm. of the seventh rib and 2 cm. of each of the sixth and eighth ribs were removed. A retropleural tumor was easily felt in the costovertebral gutter. The pleural cavity was then entered and adequate exposure was obtained by aid of a rib spreader. The tumor was separated from the parietal pleurae by blunt digital dissection. It was tense, spherical, and completely encapsulated. Its pedicle was then visualized and excision was completed by use of multiple clamps, sharp dissection, and adequate hemostasis. During

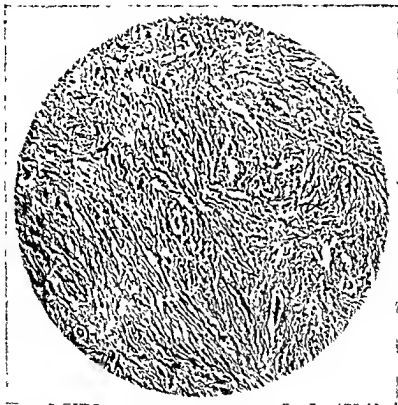


Fig. 5.—Photomicrograph of neurofibromatous tissue

removal the sympathetic chain and the seventh and eighth intercostal nerves appeared closely associated with the mass. Five grams of sulfathiazole powder and 50,000 units of penicillin were applied in the thoracic cavity. The chest wall was closed in layers without drainage, using interrupted sutures of fine black silk during gradual reexpansion of the right lung. The immediate postoperative condition was excellent. A transfusion of 500 cc. of whole blood was given during operation. Recovery was uneventful. The patient began to walk on the third day and left the University Hospital on July 5, the seventh postoperative day. He has remained entirely well to date. There have been no dyspnea or choking spells. Nervousness has disappeared. He has regained normal weight. Radiograms at six months (Fig. 2) and at twelve months following operation revealed no abnormalities except for the excised segments of the sixth, seventh, and eighth ribs.

The tumor (Fig. 3) as removed weighed 60 Gm. It was spherical, smooth, well encapsulated, and measured 6 cm. in diameter. The cut surface (Fig. 4) had a variegated appearance showing areas of old hemorrhage, cyst formation, and yellow tissue in a background of firm grayish tissue. Microscopic examination revealed wide variation in the appearance of various serial sections. Hemorrhage and xanthomatous degeneration as well as degenerative changes presumably due to the x ray therapy were prominent. However, quantitatively the most representative tissue is reproduced in Fig. 5, which is a neurofibroma as shown by special silver staining.

#### SUMMARY

Röntgenotherapy elsewhere proved futile in the treatment of this mediastinal neurogenic tumor. However, surgical extirpation four years later was relatively easy and proved curative.

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## CURARE AND SHOCK: THE PRODUCTION OF HEMORRHAGE INTO THE UPPER INTESTINE OF THE DOG WITH LARGE DOSES OF CURARE

FRANK COLE, M.D.,\* DULUTH, MINN., IVAN D. BARONOFKY, M.D.,† AND  
OWEN H. WANGENSTEEN, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School)

CURARE and its alkaloids now are being employed to produce and improve skeletal muscular relaxation during anesthesia for various abdominal operative procedures. In this laboratory recent investigations by one of us (F. C.) of the effects of very large doses of curare in dogs revealed an interesting finding: intense submucosal and mucosal congestion of the entire small and large intestine, with free bleeding into the intestinal tract.<sup>1</sup> The stomachs of these animals did not appear to be congested. Recently, it has been shown that histamine-provoked ulcer or erosion may be accelerated greatly in the experimental animal by venous congestion.<sup>2</sup> The objects of this study were the determination of the mechanism of the development of the intestinal congestion and bleeding, a more detailed examination of the pathologic changes produced by large doses of curare, and an exact knowledge of the effect of large amounts of curare on blood pressure in the experimental animal.

These experiments were performed on eighteen dogs. Intocoestrin, a preparation of curare,‡ was used throughout. All injections were intravenous; the entire amount always was given at once, and rapidly. Doses ranged from 0.035 to 1.333 c.c. of Intocoestrin per pound of body weight.

**Experiment 1.**—One Pavlov and two Heidenhain pouch dogs were used. They had been fasted previously for seventeen hours. After fasting, samples were collected, the drug was injected, and specimens were taken. Body weights ranged from 25 to 53 pounds, Intocoestrin doses varied from 1.0 to 2.0 c.c. Drooping of the head due to cervical muscle relaxation was encountered in all cases, the animals being suspended in slings. Intercoastal muscle paralysis commonly was seen. Cyanosis was present in two cases. A total of three readings was made on the Heidenhain pouch dogs and two on the Pavlov dog. While doing a fourth reading on one of the Heidenhain pouch dogs, the animal died from respiratory paralysis. It was found that there was no stimulation of volume or of free hydrochloric acid in the gastric secretions in the Heidenhain or Pavlov pouch dogs.

**Experiment 2.**—In two dogs, 10 c.c. of Intocoestrin were poured into the jejunum (opened along the antimesenteric border) under intravenous pento-

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\*Department of Anesthesiology, St. Mary's Hospital.

†National Cancer Trainee.

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barbital sodium (15 mg. per pound) anesthesia. The Intocostin was kept there for one-half hour. No bleeding or congestion was noted.

*Experiment 3.*—Three dogs, whose weights ranged from 22.5 to 43 pounds, were given Intocostin, in doses from 0.718 to 1.240 c.c. per pound. Tracheal intubation was performed immediately, and artificial respiration was instituted promptly and maintained continuously until the animal died. Entry of the gastric secretions into the duodenum was prevented by putting a strong ligature around the pylorus as soon as possible after curarization (four to ten minutes). In one case a ligature was placed below the entrance of the major pancreatic duct to prevent bile and pancreatic secretions from continuing to enter the small intestine. These dogs died in two to five hours, larger doses of curare being associated with shorter survival times. In all three animals bleeding was found in the small bowel; the hemorrhage was characterized by a gradient, being most marked in the duodenum and least in the ileum. No blood was found in the large intestine. Where ties had been placed between the stomach and duodenum and below the ampulla of Vater, the closed duodenal loop was found to be intensely hemorrhagic, as was the entire jejunum and ileum. In this animal the appendix was markedly hemorrhagic.

*Experiment 4.*—Minimal lethal doses of curare (0.065 and 0.067 c.c. of Intocostin per pound of body weight) were administered to two dogs. Artificial respiration was not performed. Post-mortem examination of these animals revealed (1) normal intestines and (2) apparently an increased amount of intestinal secretions, particularly in the small bowel.

*Experiment 5.*—Pentobarbital sodium solution (15 mg. per pound) was injected intravenously in two dogs. The trachea was promptly intubated, using a wide bore rubber tube with an inflatable cuff, and continuous artificial respiration was instituted immediately. A cannula was then inserted into the right common carotid artery and kymographic blood pressure recordings were made. Massive doses of Intocostin (1.3 and 1.4 c.c. per pound) were injected. Immediately following (within five seconds) the injection of curare, the arterial blood pressure fell from 165 and from 130 mm. Hg, systolic to 10 to 12 mm. Hg. The blood pressure fall then continued at a slower rate until no pulse or pressure existed, death occurred in twenty-two minutes in one case and sixty-eight minutes in the other (Fig. 1). Gross autopsy findings included the following: (1) normal stomach, (2) bleeding and congestion in the small intestine, most marked in the duodenum and upper jejunum and least in the ileum, (3) apparently normal large bowel, (4) congestion of the pancreas and spleen, and (5) bilateral pulmonary atelectasis and congestion.

*Experiment 6.*—Using two dogs, the technique carried out in Experiment 5 was repeated. When the fall in blood pressure occurred following the administration of curare, ephedrine and epinephrine solutions were administered intravenously (and intramuscularly before curarization) in amounts sufficient to eliminate shock. It was found that very large amounts of vasoconstricting drugs were required to prevent the occurrence of shock. In one dog, 110 mg. of ephedrine and 4 mg. of epinephrine were administered within two hours.

It was noted that (1) the blood pressure could always be raised by the administration of a vasoconstricting agent, (2) the stimulation of blood pressure lasted only one or two minutes at times, and (3) epinephrine produced a more effectual blood pressure rise than ephedrine (Fig 2). The animals were sacrificed in two and in four hours. At autopsy, some pulmonary atelectasis and congestion were seen; the intestines appeared to be normal.

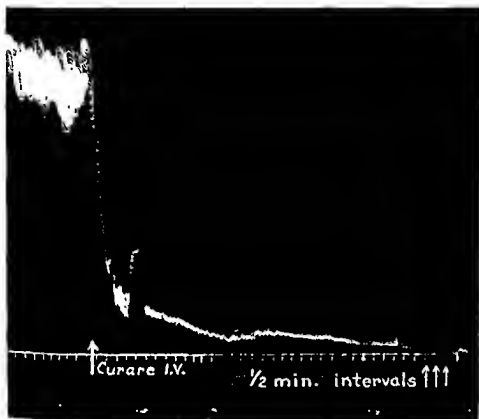


FIG 1.—Effect of large dose of curare on arterial blood pressure

*Experiment 7.*—Two dogs weighing 14 pounds were anesthetized by the intravenous injection of sodium pentobarbital. Each then received 3 c.c. of heparin intravenously. A needle was inserted into a vein and connected to a manometer, then 10.5 c.c. of Intocostin (0.750 c.c. per pound) were administered intravenously in each case, and artificial respiration was performed. No change in venous pressure occurred following curarization. Venous pressures varied between 6 and 8 cm. Post-mortem examination showed congestion of the intestines in both dogs. One animal had atelectasis of one lobe, the other had a patchy atelectasis of both lungs.

*Experiment 8.*—A dog weighing 20 pounds received 400 mg. of sodium pentobarbital intravenously. The trachea was intubated and an artery was

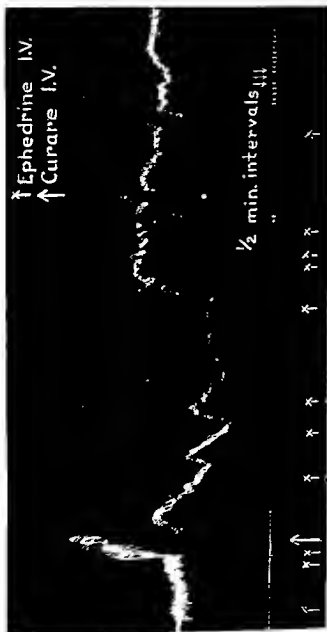


Fig. 2.—Record of arterial blood pressure after administration of massive dose of curare, where vasoconstricting drugs were administered

cannulated. A blood transfusion was started very slowly. Three cubic centimeters of heparin were injected intravenously to prevent clotting in the venous pressure tube, eliminating the need for citrate solution. A venous pressure apparatus was set up; the reading at this time was 12 cm. Just after the flow of blood was increased, 15 c.c. of Intocostrin were injected intravenously so that it passed through the drip bulb in a steady stream. The arterial blood pressure fell rapidly to 10 mm. Hg, then gradually to zero. At this time, while artificial respiration was being performed, the venous pressure rose slightly, to 2.5 cm. Three hundred cubic centimeters of whole blood were injected.



Fig. 3.—Small intestines of dogs receiving 10 c.c. of Intocostrin per pound and continuous artificial respiration. Note hemorrhage and engorgement of stasels ( $\times 80$ ).

The same technique was carried out in a dog weighing 16 pounds. This animal was given 12 c.c. of Intocostrin (0.750 c.c. per pound). It was found immediately following curarization that there was considerable difficulty in inflating the lungs. The arterial blood pressure fell immediately on curarization; the venous pressure rose gradually and steadily to 18 cm. During this time about 325 c.c. of whole blood were injected rapidly in ten to fifteen minutes.

Microscopic studies of sections of various splanchnic viscera (stomach, intestines, pancreas, spleen, liver, lungs, adrenals, and kidneys) in the dogs receiving lethal doses of curare and artificial respiration in Experiments 3, 5, and 6 revealed interesting findings. Those animals given intravenous curare and artificial respiration, with no attempt being made at raising the blood pressure (Experiments 3 and 5), showed intense engorgement of the intestinal



capillaries and venules of the mucosa and submucosa (Fig. 3). The only organs studied that were not affected were the adrenals and stomach. In those animals receiving a vasoconstricting drug in addition (Experiment 6), no gross or microscopic evidence of hemorrhage or congestion was seen (Fig. 4). The lungs, however, appeared congested. These findings were in contrast to those in the animals in which the blood pressure was allowed to fall. The dogs receiving apneic doses of curare showed no congestion.



Fig. 4.—Intestines of dogs receiving massive doses of curare where vasoconstricting drugs were administered ( $\times 80$ ).

#### COMMENT

The lack of stimulation of gastric secretions by somewhat larger than therapeutic doses of curare (0.035 to 0.040 c.c. of Intocostin per pound) and the consistent finding of mucosal intestinal hemorrhage and congestion after exclusion of gastric juice as well as after the simultaneous exclusion of gastric, biliary, and pancreatic digestive juices from the jejunum suggest that the intestinal bleeding and congestion caused by such doses of curare are not brought about by the digestive secretions. That the intestinal congestion is not due to a local effect of curare was demonstrated in Experiment 2. It was shown in Experiment 4 that very large amounts of curare were required to produce the pathologic changes described; smaller (minimal lethal) doses produced no such changes. It must be noted, however, that the deaths following

these smaller doses occurred within thirteen and thirty minutes following curarization.

Experiments 5 and 6 show that (1) injections of very large amounts of curare can produce a rapid and fatal fall in blood pressure, (2) the hypotension can be corrected by the administration of vasoconstricting drugs, and (3) intestinal bleeding occurs (when large amounts of curare have been injected) when shock is produced and does not occur when the systolic blood pressure is maintained at a level of 80 to 90 mm. Hg. The failure of the venous pressure to rise (Experiment 7) and the failure of the blood pressure to increase after rapid blood transfusion (Experiment 8) can be explained by the pharmacologic actions of curare. This drug depresses the vasomotor center and ganglia.<sup>4</sup> Thus, the potential "lake" formed by the dilatation of these organs cannot be filled fast enough, and little, if any, blood returns to the heart. The heart itself is affected by large doses of curare,<sup>5</sup> and this occurrence in itself thus will prevent a blood pressure rise after transfusion. The intestinal pathology found after the administration of very large amounts of curare thus would seem to be consequent on the production of shock and on this basis alone. Freeman and associates<sup>6</sup> have shown that in the shocked dog the superficial portion of the mucous membrane of the intestine can disappear. In fact, during periods of low blood pressure the dogs always had profuse diarrhea in which sloughs of mucous membrane could be made out. It has been shown<sup>6,7</sup> that in the dog congestion of the liver, spleen, kidneys, and intestinal mucosa are present following death caused by shock. That sometimes a considerable amount of time is required for the formation of the pathologic changes described has been demonstrated by this study and by others. Dumphy and co-workers<sup>8</sup> have shown in their study of experimental traumatic shock that intestinal hyperemia, submucosal hemorrhage, and duodenal or jejunal ulcerations were found in late shock (six to twelve hours) and were not present in early shock.

These results suggest the necessity for close scrutiny of the doses used in man. It has been shown<sup>9</sup> that the minimal lethal dose of Intocostrin in the dog is 0.065 c.c. per pound of body weight. If artificial respiration is performed, pathologic changes appear with doses of 0.650 c.c. per pound (possibly earlier). Dogs can be killed by doses of 1.3 c.c. per pound, even when artificial respiration is maintained. In man, 0.025 c.c. of Intocostrin per pound<sup>2</sup> is commonly injected; as much as 0.20 c.c. per pound has been administered, although not at once. Doses sufficient to produce muscular relaxation and respiratory depression appear to be nearly alike, in proportion to body weight, in man and in the dog; the dog, however, seems able to withstand anoxia better.

#### CONCLUSIONS

1. Large doses of curare (0.718 to 1.240 c.c. per pound), when administered intravenously in single injections to dogs kept alive by artificial respiration for two to five hours, produce congestion and hemorrhage in the intestinal mucosa.

2. Curare does not stimulate gastric secretion.

3. Exclusion of the gastric juice from the intestine does not prevent the mucosal intestinal hemorrhage.

4. The topical application of curare to the mucosa of the small intestine does not produce gross congestion.

5. Dogs receiving large doses of curare exhibit severe depression of arterial blood pressure but no appreciable change in venous blood pressure.

6. Vasoconstricting drugs obviate the fall in blood pressure attending the intravenous injection of large amounts of curare; rapid transfusions of whole blood lack this effect.

7. When shock is averted, intestinal hemorrhage is not seen. Shock is therefore the most likely cause of the intestinal hemorrhage attending the intravenous injection of large amounts of curare.

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## POSTOPERATIVE PROTEIN DEFICIENCY

### WITH SPECIAL REFERENCE TO THE CANCER PATIENT

H. M. WILEY, M.D.,\* COLUMBIA, MO.

(From the Department of Surgery, Ellis Fuchel State Cancer Hospital)

A GREAT deal of investigation has been carried out during the last few years on serum protein. Due to this work it has become increasingly evident that low serum protein can, and does, lead to many clinical complications, some of serious nature. The resulting ill effect of hypoproteinemia in the postoperative case has increasingly put the surgeon on guard. Among these complications the following may be noted:

1. The healing of wounds is retarded in the presence of low serum protein. The growth rate of fibroblasts in wounds is increased by high protein diets.<sup>1</sup>
2. Actual wound disruption may, at times, be due to hypoproteinemia.<sup>2</sup>
3. The relationship of edema to this condition is well established. The surgeon should remember that clinical edema, usually, does not appear until approximately a 10 per cent increase in body weight has occurred.<sup>3</sup>
4. A decreased gastrointestinal motility may result from a hypoproteinemic state, and actual obstruction may occur about an intestinal anastomosis, because of local edema resulting from a low blood protein.<sup>4</sup>
5. Increased susceptibility to the toxic effects of anesthesia may be due to low serum protein.<sup>5</sup>
6. Susceptibility to infection is, also, increased by this biologic imbalance and, as has been shown by Whipple<sup>6</sup> and others, infection may check completely the plasma protein production.

From these, the surgical importance of hypoproteinemia becomes apparent. The studies presented here show the high incidence of postoperative hypoproteinemia, especially as it occurs in cancer patients.

*Method and Result of Study.*—A total of fifty-seven patients who underwent surgical procedures were studied. Forty-five of these operations were for cancer and twelve were for benign conditions, but all were major procedures. The average age in this group of patients was 57.6 years. Preoperative serum protein determinations were obtained and, at least, three total and fractional measurements were made within the first ten postoperative days. Twenty-one of the cancer patients had determinations made of the liver functions, as measured by the Quick hippuric acid liver function test.<sup>7</sup> Throughout the study, hydration of these patients was carefully maintained by accurate intake and output records, plus hematocrit determinations in most cases. Caution should be observed in interpreting serum protein values, because of the possible influence of dehydration. Not infrequently, patients have been seen with ap-

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\*Trainee, National Cancer Institute, and Resident in Surgery

TABLE I. NUMBER AND TYPES OF OPERATIONS WITH THE PREOPERATIVE TOTAL PROTEIN AND THE MAXIMUM DECLINE OR RISE IN SERUM PROTEIN IN THE FIRST TEN DAYS POSTOPERATIVE\*

OPERATION	PREOPERATIVE SERUM PROTEIN	MAXIMUM NUMBER OF GRAMS LOSS OR GAIN IN SERUM PROTEIN POSTOPERATIVE	
		MALIGNANT CONDITIONS	BENIGN CONDITIONS
Large bowel procedure, abdominoperineal rec- tal resection (one-stage (10))	6.2	- 1.5	
	6.1	- 1.6	
	7.1	- 2.6	
	7.7	- 2.4	
	6.3	- 1.7	
	6.4	- 1.5	
	6.5	- 2.3	
	6.4	- 0.4	
	6.0	- 1.6	
	6.2	- 1.2	
Two-stage abdominoperineal rectal resections			
(1)			
First stage	7.0	- 1.2	
Second stage	8.0	- 2.8	
Right colectomy (1)	5.7	+ 0.6	
Sigmoid colon resection (1)	6.7	- 2.0	
Cecostomy (1)	7.7	- 2.1	
Transverse colon resection (1)	7.4	- 2.9	
Radical mastectomies (12)			
	6.4	- 0.6	
	8.1	- 2.4	
	6.6	- 2.6	
	7.4	- 2.7	
	6.2	- 2.0	
	6.6	- 2.2	
	5.5	- 1.7	
	6.3	- 0.8	
	7.5	- 1.7	
	6.8	- 0.9	
	6.7	- 0.4	
	7.2	- 1.6	
Subtotal gastric resections (6)			
	6.1	- 0.7	
	7.9	- 3.2	
	4.7	+ 3.7	
	6.7		- 1.4
	5.0		- 1.2
	5.9		+ 1.2
Exploratory laparotomy (3)			
	4.9	- 0.1	
	5.4	- 1.0	
	5.6		- 0.9
Radical neck dissection (5)			
	7.6	- 0.2	
	7.0	- 2.0	
	5.3	+ 1.2	
	6.8	- 0.7	
	6.2	- 1.3	
Jaw resection (2)			
	6.9	- 2.1	
	6.1	- 1.5	
Gynecologic procedures (5)			
	7.4	- 2.1	
	6.6	- 1.4	
	6.2		- 1.6
	6.1		- 0.5
	7.2		- 1.4

\*Minus or plus sign indicates fall or rise, respectively, in serum protein from the preoperative level.

TABLE I—CONT'D

OPERATION	PREOPERATIVE SERUM PROTEIN	MAXIMUM NUMBER OF GRAMS LOSS OR GAIN IN SERUM PROTEIN POSTOPERATIVE	
		MALIGNANT CONDITIONS	BENIGN CONDITIONS
Subtotal thyroidectomy (2)	6.1 6.8		- 1.6 - 1.5
Biliary tract (1)	7.5		- 2.5
Nephrectomy (1)	6.3	- 0.8	
Axillary dissection (1)	7.3	- 0.3	
Excision of esophageal diverticulum (1)	7.1		- 1.3
Hemipelvectomy (1)	6.3		+ 2.2
Bilateral groin dissection (1)	6.1	- 1.4	
Total		45	12

parently normal, or even elevated, total protein values which show a marked fall following proper hydration. A loss of 6 per cent or more of body weight is necessary before clinical dehydration is apparent.<sup>4</sup> In Table I are listed the number and different types of operations that were studied; the maximum drop or gain in total proteins during the first ten days after operation is shown.

Of the forty-five patients with cancer, twenty (44 per cent) had total protein values below 6.5 Gm per cent on admission. Robillard and Shapiro<sup>9</sup> found 55 per cent of their cancer patients, upon whom surgery was contemplated, to have values below 6.5 Gm per cent. In studies on gastric carcinoma, Abel and co-workers<sup>10</sup> found 59 per cent with abnormally low serum protein levels. Of six gastric carcinomas explored or resected in this group, four had total protein values below 6.5 Gm per cent.

Of the forty-five patients operated on for malignancy, forty-two (93 per cent) showed a postoperative drop in serum proteins. In twelve patients not having cancer, ten (83 per cent) showed a fall in serum proteins. Casten and co-workers<sup>8</sup> have noted the following incidence of decline in plasma protein in benign conditions: Appendectomy for acute appendicitis showed a decrease in 69.6 per cent of the cases, and cholecystectomy, for cholecystitis or cholelithiasis, 81.6 per cent.

Of the forty-two cancer patients showing a postoperative fall in total proteins, the decrease was due to a drop in the albumin fraction in sixteen cases, to globulin decline in seven cases, and to a fall in both albumin and globulin in nineteen cases (Table II).

TABLE II. DECLINE OF TOTAL PROTEIN DUE TO ALBUMIN, GLOBULIN, OR ALBUMIN AND GLOBULIN

SERUM PROTEIN FALL DUE TO	NUMBER OF PATIENTS	
	(42)	PER CENT
A. Albumin	16	38
B. Globulin	7	16.7
C. Albumin and globulin	19	45.3

Kagan<sup>11</sup> has found that a decrease in total protein concentration below normal is due, almost invariably, to a decrease in the albumin fraction. Elman and Lischer<sup>12</sup> have also emphasized this. The observations made here do not entirely verify their conclusions, as the globulin fraction, also, fluctuates, especially if there is an associated infection. Of sixteen patients who had foci of infection in either the chest, or wound, or a phlebitis, twelve showed a rise in the globulin fraction postoperatively. Kagan<sup>11</sup> has stressed the relationship of hyperglobulinemia to infection.

The fact that twenty-six or approximately 61 per cent (sum of B and C, Table II), of these patients showing a serum protein fall had a decrease in the globulin fraction emphasized the clinical significance of the work of Cannon and associates<sup>14</sup>. They have directed attention to the role of globulin (especially the gamma fraction) depletion to reduced resistance to infection, and the origin of globulin from dietary amino acids.

The greatest postoperative rise in serum protein was 37 Gm. per cent. This rise was due to a marked increase in globulin, from 19 Gm. preoperatively to 57 Gm. per cent on the ninth postoperative day. Roentgenograms of this patient's chest at the time showed an extensive bronchopneumonia.

The greatest decline in serum protein in this study was 3.2 Gm. per cent, occurring in a patient after a gastric resection for carcinoma. This patient's preoperative serum protein studies showed a total of 7.9 Gm. per cent, with a fractional breakdown of albumin 3.8 Gm. per cent, and the globulin 4.1 Gm. per cent. The greatest recorded drop occurred on the fifth day after operation with a total of 4.7 Gm. per cent, made up of 3.4 Gm. per cent albumin, and 1.3 Gm. per cent of globulin. It will be noted that the decrease is primarily due to a fall in the globulin fraction. This patient's postoperative course was uneventful, with the greatest temperature elevation being 100.4° F. on one occasion. These findings emphasize the need of obtaining fractional serum protein determinations.

Only fifteen (35 per cent) of the forty-two cancer patients who showed a decline in serum protein postoperatively had recovered their initial total protein by the tenth day after surgery.

Of the cancer patients showing a postoperative decline in total protein, the average fall was 1.33 Gm. per cent by the third day, 1.32 Gm. per cent by the fifth day, and 1.17 Gm. per cent by the tenth day; and of the benign conditions showing a postoperative fall, the average decline was 0.98 Gm. per cent on the third day, 1.03 Gm. per cent on the fifth day, and 0.76 Gm. per cent on the tenth day after surgery (Fig. 1). This observation shows a slightly greater decline in serum protein concentration in cancer patients than in patients with noncancerous lesions. From this study, it is not possible to say how long it takes for the serum total protein to return to normal levels after operation.

Operations on the gastrointestinal tract, for malignant lesions, showed a decline in serum protein postoperatively in eighteen out of twenty cases. Of the ten one-stage abdominoperineal resections, all but one patient showed a drop of over 1 Gm. in the total serum protein level. Five of these had regained their

preoperative level by the tenth postoperative day. Twelve patients with radical mastectomies showed a total protein decline ranging from 0.4 to 2.7 Gm. per cent after operation. Of this latter group, only two had recovered the preoperative total protein level by the tenth postoperative day.

The small per cent of patients showing recovery within ten days, to the preoperative serum protein level, after radical mastectomy is of interest, as they are usually taking a surgical soft diet on the first day after operation and are frequently on a regular diet by the second day. It follows that these patients are on an insufficient caloric intake for only one or, at most, two days after surgery. Accordingly, it is felt that starvation per se does not entirely account for the postoperative decline in total serum proteins following radical mastectomy.

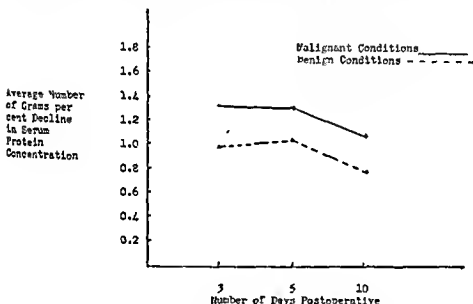


Fig 1—Average fall in serum proteins on third, fifth, and tenth postoperative days

In patients who have undergone a major surgical procedure there is frequently considerable blood loss, which may partially account for the total serum protein fall. Of thirty-one cancer patients, in whom both preoperative and postoperative hemoglobin determinations were available, twenty-seven patients showed a fall both in hemoglobin and in serum protein. Four patients showed a rise in hemoglobin and a fall in the serum protein. All of those who showed a rise in hemoglobin received one or more blood transfusions during, or immediately after, operation. Collier and co-workers<sup>22</sup> reported on the blood loss following various operative procedures. In radical mastectomies they found an average loss of 732 c.c. in twenty operations, compiled from various authors' reports. As stated previously, all radical mastectomies in this study showed a postoperative decline in serum protein concentration. Many of these patients were in an excellent state of nutrition, which might suggest that the serum protein drop was largely due to blood loss per se. However, if the ratio of one



to thirty<sup>12</sup> of serum protein to body protein is remembered, even a loss of several hundred cubic centimeters of blood will not account for the entire fall in serum protein in all cases. Whipple<sup>13</sup> has shown that a "dynamic equilibrium" exists between the body and blood proteins, the body giving up protein to the blood stream when blood is lost, so that the one to thirty ratio is maintained. Thus, if 700 c.c. of blood are lost, and the preoperative serum protein level was 7 Gm. per cent, this would represent a loss of 49 Gm. of protein. It can be calculated that an individual weighing seventy kilograms would have to lose 75 Gm. of protein to reduce the serum protein to 5.5 Gm. per cent. In the twelve radical mastectomies studied here, eight patients showed a loss in serum protein greater than the calculated loss from bleeding at operation alone, the differences being quite marked in several cases (Table III). From these findings it is apparent that the blood loss at operation does not entirely account for the total serum protein loss. The explanation of this loss is not entirely known. However, it is felt<sup>14</sup> that the more important factors are a decreased protein intake and an enhanced protein catabolism. Elman<sup>15</sup> has shown that most fasting patients excrete about 4 to 5 Gm. of nitrogen a day when sufficient glucose is ingested to meet the calorie needs. Postoperatively, he noted a rise in urinary output of nitrogen in some cases to as much as 26 Gm. per day. This would correspond to the catabolism of 162.5 Gm. of protein. The influence of anesthesia may bear some relationship to postoperative serum protein decline and should be investigated.

TABLE III DIFFERENCE BETWEEN THE CALCULATED PROTEIN LOSS FROM BLEEDING AT OPERATION AND THE ACTUAL PROTEIN LOSS

PATIENT	WEIGHT (IN KG.)	PREOP. SERUM PROTEIN (GM. PER CENT)	MAXIMUM POSTOP. SERUM PROTEIN DROP (GM.)	CALCU- LATED BLOOD VOLUME IN C.C. ( $\frac{1}{12}$ OF BODY WEIGHT)	CALCU- LATED PROTEIN LOSS FROM BLEEDING (GM.)	ACTUAL PROTEIN LOSS (GM.)	DIFFERENCE BETWEEN BLEEDING LOSS AND ACTUAL LOSS (GM.)*
27	60	6.6	2.2	4,600	46.2	101.2	55.0
53	50.8	7.4	2.7	3,900	51.8	103.3	51.5
35	96.3	8.4	0.6	7,300	41.8	43.9	+1.00
44	77.7	6.6	2.6	5,900	42.2	153.4	111.2
1	53.1	6.7	0.4	4,400	46.9	17.6	+29.3
22	67.2	6.8	0.9	5,100	47.6	45.9	+1.7
33	59	7.8	1.7	4,400	55.6	74.8	19.2
32	63	8.1	2.4	5,300	56.7	127.2	70.5
6	64.5	7.3	1.6	4,190	51.1	67.06	15.96
17	62.7	6.4	1.7	4,820	44.8	81.94	37.14
9	65.9	6.3	0.8	5,070	44.1	40.56	+3.54
29	63.6	6.3	2.0	4,000	44.1	98.0	53.9

\*Plus sign indicates bleeding protein loss to be greater than actual loss.

It is felt that in patients with "subnormal" serum protein concentrations that the body protein reserves are, also, bordering on depletion. When such a patient is subject to an acute nutritional emergency, for example, operation, traumatic injury, and anesthesia, and the resulting enhanced protein catabolism, the body protein reserve is quickly exhausted and is reflected in a lowered serum protein concentration. In contrast to this acute nutritional insufficiency, a

chronic caloric deficiency may not be reflected by the serum protein level for some time, because of the relatively slow exhaustion of the body protein reservoir.

Of twenty-two patients who had preoperative and postoperative hippuric acid determinations, no conclusive relationship between changes in liver function, as measured by this test, and variations in the serum protein were apparent. Casten and associates<sup>3</sup> in a large group of patients, found that the presence of subnormal hippuric acid excretion was of value in predicting postoperative protein decline.

It is known that the various amino acids are metabolized in different ways by different tissues, for their own specific needs, producing muscle protein, hormones, etc.; others are deaminized in the liver or kidney.<sup>19</sup> Accordingly, it is felt that of the many liver function tests, each measures only one specific function of that organ, and none of the present known tests specifically measure the ability of the liver to utilize proteins; there are no known tests for measuring the ability of other tissues to utilize protein.

*Treatment.*—In the treatment of the hypoproteinemic state, two factors must be considered: one, the lowered serum and body protein, and two, the impaired liver function which may be present. From a practical standpoint, it is almost impossible to provide enough protein for the body needs, except when taken by way of the alimentary tract. It is generally stated that 1 Gm. of protein per kilogram of body weight a day is necessary to maintain nitrogen balance. However, this amount will furnish only the daily requirements in a person whose previous nutrition has been adequate. Patients with a decreased protein reserve should receive more than 1 Gm. of protein per kilogram of body weight. Knowing that the ratio of serum protein to body protein is approximately one to thirty, it can be calculated that to raise the total protein from 5 to 7 Gm. per cent, in an individual weighing seventy kilograms, it will require approximately 331 Gm. of protein. If a patient ingested and assimilated  $1\frac{1}{2}$  Gm. of protein per day, per kilogram, for ten days, it would theoretically elevate the total serum protein from 5 to 7 Gm. per cent, provided sufficient calories were available from carbohydrates and fats to meet the daily requirement. Patients with a lowered protein reserve will probably, also, have depletion of their glycogen reserve,<sup>12</sup> and will require at least 3,000 calories per day. A diet of 3,000 calories consisting of 70 per cent carbohydrates, 5 per cent fat, and 25 per cent protein will provide an excess of protein and can be readily assimilated. The experience of Cuthbertson<sup>20</sup> is of note, as he was unable to eliminate the period of postoperative negative balance, with diets containing as high as 230 Gm. of protein and 4,100 calories.

All too frequently it is impossible for patients to take an adequate diet by mouth preoperatively and for a varying number of days postoperatively. In these cases one is left with two alternatives, jejunal alimentation or parenteral replacement.

Jejunal alimentation is an old method of feeding, which has recently been re-emphasized by Colp and Druckerman.<sup>21</sup> This method of feeding consists of placing a catheter in the upper jejunum (Witzel procedure). After twenty-

four to forty-eight hours patients can be fed a liquid diet through this tube. It may be done as a preliminary procedure to prepare patients for subsequent surgery or as a complementary procedure at the time of surgery. Experience here has not found it possible to prevent postoperative serum protein decline by jejunal feeding, nor, when used as a preliminary procedure, to raise appreciably the serum protein concentration.

A number of good formulas are available for tube feeding. Colp and Druckerman<sup>21</sup> used the Scott-Ivy formula. A recent product,\* prepared by a commercial house, would be excellent for this purpose. It yields 47 calories per gram. It was originally prepared as a food for undernourished infants and is marketed as such.

The formula used for the experiments described in this paper is shown in Table IV. This formula has proved quite satisfactory without causing diarrhea, distention, or other notable ill effects. It contains approximately 15 calories per cubic centimeter. Vitamin concentrates may be, and frequently are, added.

TABLE IV. FORMULA FOR TUBE FEEDINGS

	GRAMS OF PROTEIN	NUMBER OF CALORIES
Egg white (4)	12	208
Egg yolks (4)		
Milk (1,000 c.c.)	30	675
Evaporated milk (210 c.c.)	17.5	311
Plain malt ( $\frac{1}{2}$ lb) $\frac{1}{2}$ lb.	10.0	307
Dextrin ( $\frac{1}{2}$ lb) or	---	307
Sugar ( $\frac{1}{2}$ lb) 250 Gm.	---	301
Orange juice (or 100 c.c. tomato juice)	1.2	40
Total	70.7	2,309
Makes a total of 1,500 c.c.		
Cook first four ingredients as soft custard.		
Add orange or tomato juice after cooking; strain.		
Add vitamin concentrates if desired.		
One cubic centimeter equals approximately 1.5 calories.		

Abbott,<sup>22</sup> in discussing feeding mixtures for use in jejunal alimentation, has stressed the following points. (1) The normal fasting jejunal contents are hypotonic. (2) The maximal glucose concentration that normally enters the duodenum, from the stomach, is 15 per cent. (3) The maximal sugar concentration obtained from the jejunum, after glucose ingestion, is 6 per cent. (4) Hyperperistalsis is produced by the introduction into the intestines of any glucose solution, in excess of these values. (5) In general, low concentration of amino acid and fatty acids are present in the jejunum. "In a word, it seems desirable to predigest the food to avoid the risk of there being inadequate ferments for digestion, in the sick patient. . . ."<sup>23</sup>

It has been found desirable to use a 5 per cent casein digest, plus a 5 per cent glucose mixture in jejunal feeding, for the first three or four postoperative days, since there is a decreased secretion of digestive ferments after abdominal surgery. This should be given in amounts, not in excess of 30 to 60 c.c. every one or two hours, to avoid distention of the bowel.

\*Nutramigen, consisting of dextrimaltose, amigen, neutral fat, arrowroot starch, calcium gluconate, brewers' yeast, and minerals added to simulate the quantities present in cow's milk; manufactured by Mead Johnson and Company, Evansville, Ind.

A number of protein-containing fluids are available for parenteral use. In Table V are listed those that are in common use

Whole blood is essential where there is both an anemia and a hypoproteinemia. Frequently, two, three, or more whole blood infusions will be necessary to correct the anemia. Whipple<sup>8</sup> has found that if there is both an anemia and a hypoproteinemia present in dogs, that the protein fed first replaces the protein fraction of hemoglobin. Accordingly, it is felt that in all operations in which there is considerable blood loss, this should be replaced by transfusions of whole blood.

After anemia is corrected, one of the fluids listed in Table V can be used. It is generally accepted that plasma is the best source of parenteral protein for elevation of low serum protein. It should be re-emphasized that even with plasma it is not practical to give large enough amounts to raise a markedly decreased serum protein. Strumia and co-workers<sup>23</sup> have calculated the need in severely hypoproteinemic patients, during the preoperative and postoperative periods, who can take little food orally, at 13 L of plasma, or the equivalent of fifty-three donors. Its chief value is in the treatment of shock and during the first few days after operation, when it may partially meet the body protein needs

TABLE V. PROTEIN CONTAINING FLUIDS AVAILABLE FOR PARENTERAL USE

- |  |
|--|
| 1. Whole blood                               |
| 2. Human blood plasma (whole or lyophilized) |
| 3. Human blood albumin                       |
| 4. Ascitic fluid                             |
| 5. Digests of casein or amino acid mixtures  |

Human albumin is of great value, especially in the presence of edema. It has been found that approximately 18 c.c. of fluid will be drawn into the blood stream for each gram of albumin given. It must be remembered, however, that it lacks fibrinogen, prothrombin, and globulin with its antibodies, and as there is a need for all of these in most patients, before and after major surgery, that shortcoming is apparent. At the present time, albumin is difficult to obtain, except in a few medical centers, and in the Army and Navy. Modified bovine albumin<sup>24</sup> or some of the intravenous gelatine<sup>25</sup> solutions, which are in the experimental stages, may eventually be the answer to meeting the body protein needs following surgery.

Ascitic fluid has been used by Davis and Getroff<sup>26</sup> to improve a low serum protein, with definite evidence of elevation. It may be given either intravenously or subcutaneously, without preliminary typing or cross-matching. In the writer's experience, however, febrile reactions of a slight to moderate degree have occurred, even when the fluid was readministered to the patient source. If ascitic fluid is to be administered intravenously, only that which is crystal clear should be used.

Casein digests, or amino acid mixtures, were apparently first used in man in 1939 by Robert Elman. The most widely used amino-acid mixture is Amigen \*

\*Manufactured by Mead Johnson and Company.

Amigen is a casein enzymatic digest containing approximately 85 per cent amino acids and 15 per cent polypeptides. Each gram yields 34 calories and 0.12 Gm. of nitrogen. The practical details involved in its preparation and use have largely been solved. Reactions are few and phlebitis is rare. A solution of 5 per cent amigen in 5 per cent glucose is apparently the most practical, and will yield 370 calories. Elman and Lischer<sup>12</sup> further stated, "... if a patient needs intravenous injections of glucose, he needs intravenous injections of amino acids even more, inasmuch as the former can be made easily from the latter, whereas there is no substitute for the nitrogenous amino-acids."

In the writer's experience reported in this paper, confined largely to patients having cancer, who have lost weight over long periods of time, it has not been possible, or practical, to prevent a postoperative fall in serum protein by the use of parenteral feeding alone, and only after the patient began to take protein by mouth was an increase in serum protein noted.

In restoration of impaired liver function four points have proved of value: high protein, high carbohydrate, low fat diet, and lipotropic substances to mobilize liver fat.

Fortunately, in general, those things that will elevate the decreased total protein will improve the liver function. The diet mentioned previously meets these requirements, mainly, 70 per cent carbohydrates, 25 per cent protein, and 5 per cent fat.

It had been known for years that a fatty liver indicates a poor liver. The normal liver contains 6 per cent by weight of fat.<sup>13</sup> There is no test available for the presence of fat in the liver, but a liver containing 10 per cent by weight of fat will generally be enlarged.<sup>14</sup> It has been found that certain substances will replace the liver fat. Several lipotropic substances have been found to be of value in mobilizing the liver fat, among these are lecithin, cephalin, choline, egg albumin, casein, gelatin, and the amino acid methionine. Dragstedt has described a very potent lipotropic, a pancreatic hormone, which he called lipocaine.

It has been shown<sup>15</sup> that the administration of amino acids to patients with cirrhosis of the liver decreases the hepatic fat and increases the percentage of proteins. This is thought to be largely due to the methionine contained in the amino acids. Beattie and co-workers<sup>16</sup> have successfully treated a patient who accidentally took 30 to 40 c.c. of carbon tetrachloride (maximum therapeutic dose 4 c.c.) with casein digest and methionine.

In general, from the clinical standpoint, it has been most convenient to supply the lipotropic substance by means of a high protein diet. Goldschmidt and associates<sup>17</sup> believed that protein has the following four modes of action in protecting the liver: (1) Probably some specific, and as yet unknown, action on the liver cell; (2) replacing fat more effectively than carbohydrate, thereby making the liver less susceptible to injury; (3) through the fact that the liver is one of the chief storehouses of protein; (4) playing the major role in regeneration, which begins seventy-two hours after the original injury to the liver (in animals subject to damage with chloroform).

Choline will decrease liver lipid content and can be given parenterally as liver extract, which has a high choline content. The vitamin B complex and, better still, brewers' yeast also exert a protective action on the liver. It has been our practice to give brewers' yeast preoperatively and postoperatively in all major surgical cases, when food is being taken by mouth. There is evidence to show<sup>21</sup> that brewers' yeast contains some unidentified substance not found in the vitamin B complexes, which is of value in hepatic damage.

In the experiments reported here, a postoperative serum protein decrease occurred in 93 per cent of patients suffering from cancer, in spite of a preoperative high protein diet, and postoperative jejunal feedings in some cases, and the liberal use of blood and plasma. The serum protein concentration rose only after the patient had been taking an adequate diet by mouth for several days.

#### SUMMARY AND CONCLUSIONS

Forty-four per cent of the cancer patients studied had a preoperative total protein value below 6.5 Gm per cent. A postoperative decline in serum protein concentration occurred in 93 per cent of the patients studied, this decline usually occurring in the first three to five days. In a small group of patients operated on for benign conditions, 83 per cent showed a fall in serum protein after operation. A postoperative decline in serum protein can be expected after most major surgical procedures.

Among the cancer patients, the postoperative decline in serum protein concentration was found to be due to albumin drop in sixteen cases, to globulin in seven cases, and to a decrease in both albumin and globulin in nineteen cases (Table II). An increase in globulin is to be expected in those patients whose postoperative course is complicated by some focus of infection. We feel that it is necessary to obtain both total and fractional serum proteins to evaluate adequately this blood constituent.

Only 30 per cent of the patients had regained their initial total serum protein concentration by the tenth postoperative day.

Evidence is presented showing that the blood loss, even at a relatively "bloody" operation such as radical mastectomy, does not entirely account for the total serum protein decline.

No correlation between the serum protein decline and liver function, as measured by the hippuric acid excretion test, was apparent in this study.

In the discussion of treatment, the difficulty of providing enough protein to prevent the postoperative serum protein decline is emphasized. It was found that, in general, serum proteins in elderly, frequently debilitated cancer patients returned to normal only after an adequate diet, by mouth, was taken for several days, only 30 per cent returning to the preoperative level within ten days after operation. The increased liver protein following the use of amino acids and methionine as suggested by Fagin and co-workers<sup>22</sup> should receive wider clinical investigation.

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## JEJUNAL MALIGNANCY

EARL A. CONNOLLY, M.D., AND ARNOLD W. LEMPKA, M.D., OMAHA, NEB.  
(From the Department of Surgery, Creighton University School of Medicine)

### INTRODUCTION

REPORTS in the literature on primary carcinoma of the jejunum indicate the lesion is not only rare but also accompanied by an unfavorable prognosis. Two cases are being reported to add to the list of those with a more favorable result following surgical intervention.

### REPORTED INCIDENCE

Swan,<sup>1</sup> in a search of the literature from 1929 to 1945, found sixty-six cases of jejunal cancer. Mayo<sup>2</sup> reported a series of forty cases from 1907 to 1939. Jetter<sup>3</sup> reported only one case over a period of nineteen years in a series of 4,308 malignancies. Boman<sup>4</sup> found three cases in 230,000 admissions to St. Luke's and St. Mary's Hospital, Duluth, Minn. Hunt and Kaneb,<sup>5</sup> reporting on 81,477 patients admitted to the Surgical Department at Worcester City Hospital from 1921 to 1928, found that out of 28,135 surgical specimens examined by the laboratory, three were carcinoma of the jejunum. Out of 2,266 autopsies, sixty-seven were carcinoma of the gastrointestinal tract but none were primary carcinoma of the jejunum. Medinger<sup>6</sup> reported twelve cases of carcinoma of the jejunum out of 1,456 necropsies and 41,000 surgical specimens. Mayo and Nettour<sup>7</sup> reported an incidence of 0.15 per cent of all carcinoma of the gastrointestinal tract to be jejunal. At Cook County Hospital, Christofferson and Jacobs<sup>8</sup> found 0.9 per cent of intestinal carcinoma to be cancer of the jejunum in 10,309 necropsies. A higher incidence was reported by Hunt and Kaneb.<sup>5</sup> They found three cases, or 2.1 per cent, out of 147 operative cases of gastrointestinal carcinoma. Brill,<sup>9</sup> in statistics covering 3,563 intestinal tumors, found 97.5 per cent were in the rectum, colon, and appendix. According to Homans,<sup>10</sup> tumors of the small intestine are very rare, more often adenocarcinoma than benign growths. The former led to a chronic sort of obstruction. Ficarra and Marshall<sup>11</sup> reported only twelve cases encountered at the Lahey Clinic in thirty years. According to Feldman,<sup>12</sup> carcinoma of the small intestine is an uncommon disease, the necropsy incidence being about 0.05 per cent. The incidence of the site of the lesion is as follows: duodenum 25 per cent, jejunum 40 per cent, and ileum 35 per cent. Harris and Rosenblum<sup>13</sup> and Carter<sup>14</sup> reported the incidence of carcinoma of the jejunum as approximately 1 per cent of all intestinal carcinomas. Nothnagel<sup>15</sup> reported nine instances of carcinoma of the jejunum in 3,585 carcinoma deaths or an incidence of 0.025 per cent. Bunting,<sup>16</sup> in 2,200 autopsies, found 104 cases of gastrointestinal cancer, four involving the small intestine and none the jejunum.



The two cases we are now reporting are the only patients with diagnosed primary malignant tumors of the jejunum admitted to St. Joseph's Hospital since 1932. Since this time, 110,965 patients have been examined in the hospital, making an incidence of 0.0018 per cent. During this time 3,631 autopsies were performed by the personnel of the pathology department of Creighton University School of Medicine. The number of carcinomas was as follows: Esophagus, 21; stomach, 55; duodenum, 3; jejunum, 0; ileum, 0; bowel, large, 45; rectum, 20.

Some theories as to the reason for the low incidence would include those given by Brooksher,<sup>17</sup> who stated that there is less irritation because of the fluid content of that portion of the bowel, the alkalinity or special inhibitory action of secretions may be a factor, and the absence of any fixed or abrupt angulations all may be contributory to the decreased incidence. Heggs<sup>18</sup> added that the lack of stasis of the contents of the area may possibly account for the rarity of the lesion.

#### AGE AND SEX

Small intestine neoplasms occur during middle age. Ewing<sup>19</sup> reported an average age incidence of 46.5 years. Mayo and Nettour<sup>7</sup> found 51.0 years the age incidence for their series. The average age in Babcock's<sup>20</sup> cases was 46 years. However, Joyce<sup>21</sup> reported a jejunal carcinoma in a 25-year-old Filipino man. The literature would indicate that the lesion occurs more frequently in men than in women. Hunt and Kaneh<sup>4</sup> found 2:1 to be the ratio of men to women in the occurrence of jejunal carcinoma. Mayo<sup>8</sup> found it to be 2½ times more common in men than in women. In our two cases one was a man, aged 40 years, and one a woman, aged 47 years.

#### SYMPTOMATOLOGY

Symptoms of a carcinoma of the jejunum are not stereotyped, but vary from little or no localizing symptoms to those manifested by severe intestinal obstruction.

Some patients, according to Martin,<sup>22</sup> complain of vague abdominal distress, much on the order of those who are classed as neurotics. Some say they are aware of a certain mobility of the intestines and a fatigue that occurs before meals. Others experience a dizziness that cannot be explained and it is often associated with an unpredictable wave of nausea. Mayo<sup>8</sup> said that the two main features are recurrent attacks of intestinal obstruction with intercurrent relief and anemia associated with weakness and fatigability. The latter, he claimed, can be explained by the direct loss of blood from the ulcerated regions. Boman<sup>4</sup> described persistent, unexplained anemia and symptoms of intestinal obstruction as the usual findings. Weakness is found early, as is easy fatigability. Usually there is a loss of weight. In the Mayo and Nettour<sup>7</sup> series there was an average weight loss of twenty-five pounds. This is probably explained by interference with normal bowel function, both in mobility and absorption. Tarry stools are seldom seen. Occult blood, however, is found if

enough stools are examined. Later, as the lumen narrows, pain may manifest itself and there may be abdominal distention with nausea and vomiting. The vomiting is usually intermittent and increases in severity as the obstruction progresses. Pain, as described by Boman,<sup>4</sup> varies from vague discomfort to severe colic located in the region of the umbilicus and lower quadrant of the abdomen. The time of pain interval is inconsistent but may occur one to two hours after eating. Pain in the epigastrium is a late symptom and is found after there is metastasis to retroperitoneal lymph nodes.

Vomiting progresses as obstruction increases and may be especially severe if the lesion is located in the upper portion of the jejunum. Constipation, a frequent symptom, may be alternated with diarrhea or even normal bowel movements. Hunt and Kaneb<sup>5</sup> mentioned salivation as a characteristic symptom which frequently precedes vomiting. Those cases that are associated with symptoms of acute intestinal obstruction with pain, distention, and vomiting are usually found to include a polypoid carcinoma, often with intussusception. Koenig and Culver<sup>23</sup> reported upon two patients sent to them with diagnosis of duodenal obstruction, but their lesions, upon operation, were found lower in the gastrointestinal tract, namely, the jejunum.

#### PHYSICAL FINDINGS

Physical findings in cases of carcinoma of the jejunum depend largely upon the stage of the disease. Boman<sup>4</sup> stated that there are very few positive findings in the early stage. Later, the patient may be emaciated or cachectic and will be anemic. Distention varies but usually is present in the later stages. Horsley<sup>24</sup> stated that the distention may be absent, even late, if the tumor is high in the jejunum but usually quite severe if the lesion is lower. Visible peristalsis and sometimes severe peristalsis may be seen if the abdominal wall is thin. A palpable abdominal mass is usually a late finding and, if it is movable, it is highly suggestive of carcinoma of the small intestine according to Brooksher.<sup>17</sup>

#### X-RAY FINDINGS

Brooksher<sup>17</sup> said that x-ray diagnosis of small bowel carcinoma has been infrequent in the past and as determined by a survey of the literature the diagnosis is usually made at the time of laparotomy. X-ray findings may help in the diagnosis by demonstrating a filling defect at the site of the lesion with a compensatory widening proximal to the obstruction or, as Mayo<sup>8</sup> said, barium is often difficult to observe in the small intestine but its use in ruling out lesions of the stomach and large bowel will be of value.

Gabor and Miller<sup>25</sup> stated that the finding of barium in the small intestine for more than eight hours warrants further effort to localize a lesion in that portion of the intestine. Although delayed emptying time of the small intestine is suggestive of carcinoma in that region, Horsley<sup>24</sup> added that avitaminosis, sprue, pellagra, and hypoproteinemia may also cause such a finding.

According to Feldman<sup>22</sup> the roentgen recognition of carcinoma of the small intestine is often difficult. A negative roentgenogram does not exclude early

cases. Its greatest value is in demonstrating an obstructive lesion. When the upper jejunum is involved, a temporary puddling of the barium is noted proximal to the stenosis. In complete obstruction, the proximal portion of the jejunum and duodenum is distended with smoothing out of Kerkring's folds.

Golden<sup>26</sup> said that a tumor arising in the wall and growing toward the serosa, as leiomyosarcoma sometimes does, would not be detected until it ulcerated through the mucosa or until it became large enough to encroach upon the lumen.

Detection of malignant tumors by roentgen examination depends upon the demonstration of a narrowing of the lumen with obliteration of the mucosal folds. No evidence of damage has been encountered from the administration of barium by mouth in the presence of disease of the small intestine, even with narrow constriction. In the small intestine the barium suspension remains fluid.

#### DIAGNOSIS

Accurate diagnosis of carcinoma of the jejunum is often very difficult, but Boman<sup>2</sup> said that inference of small bowel malignancy may be gained from a careful history, physical examination, and the laboratory findings. However, a definite diagnosis can be made only by roentgenogram, laparotomy, or autopsy. Even in the hands of skilled roentgenologists, only 25 per cent of the lesions are demonstrable. In the Mayo<sup>2</sup> series of 101 small bowel cases, only 25.7 per cent had the tentative diagnosis of small intestine lesion before operation. Although the roentgenologist is unable to demonstrate the lesion in a case presenting clinical findings suggestive of jejunal carcinoma, one is justified in doing a laparotomy in order to make a definite diagnosis. As Boman<sup>2</sup> further stated, a thorough abdominal search should be made as concurrent diseases such as cholecystitis, duodenal ulcer, etc. may overshadow the picture produced by jejunal carcinoma.

Primary malignant disease of the small intestine must be differentiated from narrowing due to inflammation. As a general rule, a malignant constriction is short while an inflammatory constriction is longer, being at least 8 to 10 cm. in length. Carcinoma ordinarily produces a short constriction, 2 to 4 cm. in length.

#### PATHOLOGY

Malignant lesions of the jejunum are usually adenocarcinoma and are similar to the type seen in the colon. Mayo<sup>2</sup> reported forty cases, with thirty-one being adenocarcinoma, two leiomyosarcoma, one epithelioma, and six in which there were no pathologic specimens. Boman<sup>2</sup> reported that 90 per cent of the carcinomas of the small intestine are of the adenomatous type, usually annular or constricting, but may be polypoid, ulcerating, and nonconstricting. Heggs<sup>13</sup> reported that the majority of the lesions are located in the proximal portion of the jejunum. Ewing<sup>12</sup> stated that tumors of the small intestine may produce polypoid outgrowths obstructing the lumen, the lesions may ulcerate early, or the main result may be stenosis from invasions of muscular or subserous coats. Often there is dilatation of the bowel above the tumor and when the tumor lies

in the upper jejunum the disease may simulate pyloric stenosis. Babcock<sup>20</sup> said the annular type arises from mucosal glands and, therefore, has the histology of adenocarcinoma.

#### PROGNOSIS

As Boman<sup>1</sup> said the prognosis of any small bowel carcinoma is discouraging whether the growth is removed or not Rankin and Mayo<sup>27</sup> reported in 1930 that no patients lived over three years and also added that one-third of them had hopeless metastases at operation McDougal<sup>28</sup> reported that resection of the small bowel is followed by 40 per cent mortality and that about 5 per cent of the patients with small bowel carcinoma have a five-year cure. Mayo<sup>2</sup> reported a higher incidence of five-year cure, giving 12.3 per cent as his figure for a series of sixty-six cases Medinger<sup>2</sup> reported on twenty-two cases from Boston sources, of which nineteen patients were operated upon with 47 per cent mortality. Of those that lived, three were well with no recurrence for periods of eleven years, three years, and less than one year In the Mayo and Nettour<sup>7</sup> report, only four out of seventy-six were alive at the time of writing, the average duration of time for those who lived was 17.6 months. Two lived seven years. Babcock<sup>20</sup> gave an operative mortality of 17 per cent and a recurrence of 75 per cent. Gateh<sup>22</sup> stated that the results of resection were almost totally bad because of the presence of early metastases Ficarra and Marshall<sup>11</sup> said that the prognosis with or without treatment is discouraging; the duration of life after resection was given as one year to seventeen or eighteen months.

#### CASE REPORTS

CASE 1 (No. 54289).—N. L., a white man, aged 40 years, entered St. Joseph's Hospital on Nov. 29, 1932, with a history of weakness, vertigo, and melena. He had been treated for peptic ulcer about five months. Physical examination revealed an exsanguinated man with some tenderness in the epigastrium. Hemoglobin was 34 per cent and red blood cells were 2,820,000. Diagnosis was made of bleeding duodenal ulcer. He was given blood transfusions, placed on an ulcer regime, and discharged three weeks later.

On Aug. 1, 1933, he re-entered the hospital with the same history, namely, weakness, vertigo, and melena. Hemoglobin was 60 per cent and red blood cells were 3,480,000. Diagnosis was again made of bleeding duodenal ulcer. He was given transfusions, placed on an ulcer regime, and discharged three weeks later. On June 8, 1938, he re-entered the hospital because of weakness, vertigo, and melena. Hemoglobin was 43 per cent and red blood cells were 2,470,000. He was again given transfusions, placed on an ulcer regime, and discharged three weeks later. He then consulted the Mayo Clinic where the diagnosis was confirmed and he was advised that if further bleeding occurred, surgery was indicated.

On Oct. 4, 1938, he re-entered the hospital because of weakness, vertigo, and melena. Hemoglobin was 37 per cent and red blood cells were 1,970,000. He was given transfusions, continued on ulcer regime, and discharged six weeks later. On Aug. 15, 1939, he re-entered the hospital because of melena. Hemoglobin was 90 per cent and red blood cells were 4,430,000. He remained in the hospital five days. On Jan. 5, 1940, he re-entered the hospital with a complaint of weakness and melena. There was a painful area over the right rectus muscle, below the umbilicus. There was a questionable mass palpable. Hemoglobin was 80 per cent and red blood cells were 4,150,000. He was treated medically and discharged two weeks later.

He was again admitted to the hospital on Feb. 5, 1941, because of weakness, vertigo, and melena. Hemoglobin was 39 per cent and red blood cells were 2,600,000. There was a palpable mass in the right abdomen. He was treated medically and discharged seven weeks later with instructions to return for an operation when his condition improved. Although, over a period of eight years, there were frequent episodes of massive hemorrhage producing weakness, dizziness, and syncope attributed to duodenal ulcer, there never was any pain, dyspepsia, nausea, or vomiting.

He reentered the hospital on May 13, 1941 for operation. The hemoglobin at this time was 106 per cent and red blood cells were 5,260,000.



Fig. 1—Photograph of surgical specimen removed showing resected jejunum and large tumor projecting from antimesenteric border

An operation was done on May 19, 1941. Under ether anesthesia, a tumor the size of a large orange was found on the antimesenteric border of the jejunum. It was resected and an end to end anastomosis was done. He was dismissed from the hospital on June 13, 1941.

*Pathologic Report*—Gross specimen revealed a resected piece of small bowel 12 cm long, with distended vessels on the surface and a firm smooth globular mass 6 cm in diameter projecting from the convex surface beneath the serosa. When the bowel was opened the lumen led into part of the projecting nodule which was soft, red, and resembled muscle. The mucosa of the bowel around the opening into the tumor was thickened and edematous. The rest of the tumor nodule was a cavity filled with fluid blood and partially lined with layers of fibrin lying on a smooth lining. (See Fig. 1.)

*Microscopic report on sections taken from the substance of the large tumor mass, the margins of the diverticulum from the bowel and from the wall of the large area containing the hemorrhage, revealed essentially the same picture. The tumor was made up entirely of large elongated cells, with hemorrhage here and there and many hyalinized small zones. There were scattered pyknotic nuclei and a rare cell containing several nuclei and giant in*

size. Both hematoxylin-eosin and Masson Trichrome stains were used. The histologic picture was one of a muscle tumor with enough growth activity to merit the designation of leiomyosarcoma of an apparently low grade of malignancy (See Fig 2)

Diagnosis was encapsulated large polypoid subserous leiomyosarcoma, grade I, of the small intestine, with diverticulum and hemorrhage into tumor

*Remarks.*—Such lesions tend to recur if incompletely removed, and metastasize late to lungs and liver. They are radioresistant. Isolated cases of permanent cure are recorded. This particular lesion was of a low grade malignancy

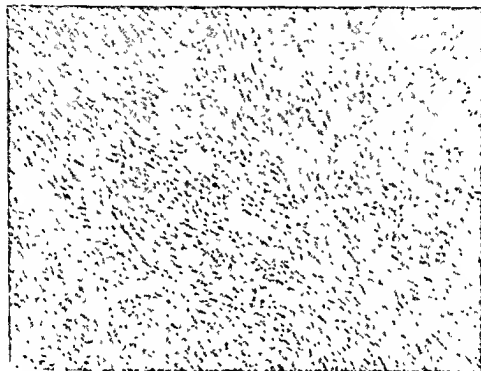


Fig 2.—Photomicrograph of leiomyosarcoma of jejunum showing elongated smooth muscle cells with some pleomorphism (low power)

The patient was examined on May 19, 1946, five years after resection of the tumor. Since the jejunal resection he has worked at his occupation as cabinetmaker, except for temporary absences, at which times a bladder stone was removed suprapubically, trans urethral resection of a hypertrophied prostate was performed, and drainage of a perinephritic abscess was done. He is in excellent health. However, he wears an abdominal support because of an incisional hernia. This will be repaired in the near future.

CASE 2 (No. 37196).—A K., a white woman, aged 47 years, entered St. Joseph's Hospital on Aug. 9, 1939, complaining of frequent vomiting and a paroxysmal type of pain in the abdomen. The patient had been in good health until about six months before admission. At that time she suffered severe pain in the abdomen, lasting two or three hours. This came on after gorging herself with popcorn. She did not vomit, but was very sick. Three months later she developed a suffocating feeling that seemed to start in the abdomen and gave her the feeling of "dying." Occasionally this was associated with vomiting. Five weeks before admission she suffered a severe vomiting attack that she attributed to the ingestion of gin, and this was the beginning of the severe sickness. She became progressively

worse and would vomit almost every time she ate. The feeling of suffocation became more and more severe. During the last month of the illness she developed a pain that often started in the region of the right costovertebral angle and radiated anteriorly to the region over the gall bladder. Vomiting recurred frequently, was projectile in character, and was accompanied by nausea. The emesis was green in color and contained particles of undigested food. There was no gross blood in either vomitus or stool, the latter, too, was said to be green. There was a loss of sixteen pounds of weight during the last two months of the illness. Past history was noncontributory.



Fig 3—X-ray picture of abdomen taken twenty-four hours after barium meal showing dilated jejunum proximal to constriction

Physical examination of the head and neck gave negative results. The chest was clear, heart regular, and there were no murmurs. Blood pressure was 174/110. There were no masses or areas of tenderness in the abdomen. She was moderately obese, weighing 171 pounds.

*Laboratory Report*—Blood count was: hemoglobin, 107 per cent (15.4 Gm. equal 100 per cent), red blood cells, 5,370,000; white blood cells, 16,600; monocytes, 1 per cent; lymphocytes, 16 per cent, neutrophils, 83 per cent; staffs, 4 per cent, segments, 79 per cent. Urinalysis showed specific gravity, 1.032; acid reaction, trace of albumin; sugar, negative. Myxomatous amorphous urate crystals. Wassermann and Kahn reactions were negative.

**X-ray Report.**—Examination of the chest was negative. Preliminary films of the gall bladder area showed no definite pathology. Esophagus was negative. The stomach filled well, action was good, negative. Pylorus and duodenum filled well, negative. In the upper portion of the jejunum there was apparently a marked degree of obstruction. Practically all of the barium was still retained proximal to this point at a seven-hour observation. Twenty-four hours later the barium had failed to pass through the obstruction previously reported in the jejunum. There was a very definite dilatation of the proximal jejunum. (See Fig. 3.)

**Treatment.**—Wangensteen suction was started; intravenous fluids, and morphine for pain, were administered for two days prior to operation. Operation was performed on Aug. 11, 1939. Through a left paramedian incision centering on the umbilicus, the small bowel was explored. Twelve inches from the duodenal jejunal junction a firm annular constricting growth was found.



Fig. 4—Photomicrograph of adenocarcinoma of small bowel invading submucosa.

**Pathologic Report**—Gross specimen was a resected piece of small bowel 8 cm. long and 3 in. in diameter. Vessels were deeply engorged. The mid portion was narrowed and within the lumen a firm mass could be felt. On opening the segment a soft gray mass filled the lumen of the central segment. It was papillary and sprang from the mucosa.

Histology revealed a papillary tumor mass in which the thin papillae were covered by one or more tall hyperchromatic epithelia. There was some invasion of the submucosa by these papillae and by glands lined by similar cells.

Diagnosis was Papillary adenocarcinoma of the jejunum, grade II. (See Fig. 4.)

**Remarks**—After an uneventful convalescence, the patient left the hospital on the twenty-first postoperative day.

Examination on May 19, 1946, six and one half years after operation, showed the patient to be entirely well and working every day. Weight is 195 pounds.



## SUMMARY

Two patients having had jejunal malignancy are reported who are alive and well five and six and one-half years after resection.

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## AMPUTATION OF THE INDEX RAY

CAPTAIN JAMES H. MAHONEY, LIEUTENANT COLONEL GORGE S. PHALEN,  
AND COLONEL WILLIAM H. FRACKELTON, MEDICAL CORPS,  
ARMY OF THE UNITED STATES

*(From the Hand Section of Surgical Service, William Beaumont General Hospital,  
El Paso, Texas)*

THE thumb is the most important digit of the hand, and the index finger ranks second only to the thumb in importance. Because the index finger is more important functionally than the other fingers, surgeons have been taught to salvage as much of this finger as possible when treating an injury to this digit.<sup>1</sup> In treating a large number of cases on a hand service of an Army general hospital, we have found that salvaging all or part of an injured index finger may often result in a loss of efficiency in the use of the hand. This is especially true when the index finger must be amputated at any point proximal to the proximal interphalangeal joint. In these cases an amputation of the index ray (index finger together with the second metacarpal bone) has resulted in a restoration of almost normal function in the injured hand. Because it is apparent that the general surgeon may not be too familiar with this type of operative procedure and its indications we feel justified in publishing this report.

We have recommended amputation of the index ray only in patients with normal, or nearly normal, function in the remaining digits of the hand. These cases fall into two groups: (1) Patients with the index finger amputated proximal to the proximal interphalangeal joint, and (2) patients with the index finger so badly damaged that any reconstructive surgery would hold little promise of restoring a fairly normally functioning digit.

The only absolute indication for amputation of a finger is loss of blood supply of sufficient severity to produce ischemic necrosis. Even though the blood supply of a finger may be adequate, amputation of the digit may be indicated if there has been sufficient damage to the tendons, nerves, and joints so that reconstructive surgery will not produce a well-functioning finger. A poorly functioning index finger of normal length may add its minimal function to the total effort of the hand, but while doing this, it also robs the remaining normal digits of a portion of their combined functions. Dexterity may be greatly impaired because of the strategic position which the injured index finger holds between the normal thumb and remaining normal fingers. If the index finger cannot be opposed strongly and painlessly to the thumb, the patient then automatically substitutes the normal long finger for this pinching action. We have observed that the long finger is capable of adequately assuming all the duties of an index finger.

Time and money may also be factors which must be considered in deciding whether a finger should be amputated or reconstructed. The patient may not be

able to afford a prolonged hospitalization or the multiple operations necessary to reconstruct a damaged finger. If the surgeon feels confident that he will be able to restore a damaged index finger to a fairly normal functional state, then the reconstructive surgery indicated should certainly be done. But the patient may lose much time and money in a vain effort to salvage an index finger which is too badly damaged ever to function normally again.

Instead of spending six to eighteen months in a futile attempt to restore the index finger to normal, the patient might find it to his advantage to submit to an amputation of the index ray and return to work within twenty-eight days.

If the index finger can be amputated through the middle phalanx, the digit will still be sufficiently long to permit an adequate pinching action between the tip of the thumb and the end of the amputated finger. Furthermore, with a normal painless range of motion still present in the proximal interphalangeal joint, the index finger will be of considerable aid in the grasping of objects. If, however, the index finger must be amputated at any level proximal to the proximal interphalangeal joint, there will remain a stump which will be of very little functional value. In fact, this short index stump actually may reduce the efficiency of the hand.

Patients who have had an index finger amputated through the proximal phalanx state that the index stump hinders the otherwise normal function of their hands. They are constantly bumping the end of the stump while doing any work with their hands. In grasping an object, the index stump may even push against the object grasped. In shaking hands, the short stump may also be in the way. There is no longer any adequate pinch between the short index stump and the thumb, and the long finger is hindered to some extent in taking over the normal function of the index finger because of the interposition of the index stump between the long finger and the thumb.

The following case reports illustrate quite well the type of patient for whom an index ray amputation is indicated.

#### CASE REPORTS

CASE 1.—A 21 year old master sergeant in the infantry was wounded in combat on Dec. 13, 1944, in Belgium. He sustained multiple wounds, including partial traumatic amputation of the right and left index fingers and the left thumb. The soldier was taken prisoner and the initial débridement and primary closure of the wounds were performed by a German medical officer. The wounds healed without infection, leaving the soldier with an amputation of the right and left index fingers through the proximal half of the proximal phalanx and an amputation of the left thumb through the base of the distal phalanx.

The soldier arrived in the United States on July 1, 1945. He was granted several convalescent furloughs, during which time he worked as a clerk and truck driver in an express agency. He was admitted to the hand service of this general hospital on Jan. 12, 1946. Examination of the right hand revealed normal long, ring, and little fingers; the thumb nail was deformed due to a minor injury in the region of the nail bed, but function of this digit was not impaired; the index finger was amputated through the proximal half of the proximal phalanx. The index finger stump was well covered with an adequate volar skin pad; there was point tenderness on the dorsoradial side of the stump. The end of the stump appeared somewhat bruised. Active range of motion in the second metacarpophalangeal joint was from 180 degrees extension to 90 degrees flexion. There were multiple small metallic foreign bodies

on the dorsum of the hand visible on roentgenogram, and three were palpable in the subcutaneous tissue over the third metacarpal and the proximal phalanx of the ring finger.

Examination of the left hand revealed normal long, ring, and little fingers. The thumb had been amputated through the base of the distal phalanx, and there was an inadequate pad over the end of the stump. The index finger had been amputated through the proximal half of the proximal phalanx, leaving a very short stump. The web between the index and

Fig. 1.



Fig. 2.

Fig. 1 (Case 1).—Dorsal view of both hands. Both index fingers have been amputated through the proximal half of the proximal phalanges, leaving very short stumps. The soldier complained that these short index stumps were constantly hindering him in the efficient performance of manual labor.

Fig. 2 (Case 1).—Dorsal view of both hands, following index ray amputations. There is no longer any obstacle between the thumb and fingers.

middle fingers had been drawn somewhat distally when the index stump was closed, but there was still active motion in the second metacarpophalangeal joint of 180 degrees extension to 90 degrees flexion. There was no point tenderness over the index stump, but the end of the stump appeared somewhat bruised.

On admission, the soldier made the following statement: "Something has to be done with these forefinger stumps, as they are always in my way. I bump them so often they get tender."

On Jan. 19, 1946, the soldier had bilateral index ray amputations with plastic revision of the amputation stump of the left thumb and removal of the three palpable metallic foreign bodies from the dorsum of the right hand. The operative incisions healed by primary intention. On the twenty-first postoperative day, active motion of the fingers and wrist was instituted. Physical therapy, consisting of whirlpool baths and massage, was given for one week to aid in the return of normal motion in the fingers of both hands. On the twenty-eighth postoperative day, the soldier was discharged from the Army on a certificate of disability. He returned to his former civilian occupation as a clerk and truck driver in an express agency, and at this time he is performing the work much more efficiently than he could prior to amputation of the index rays.

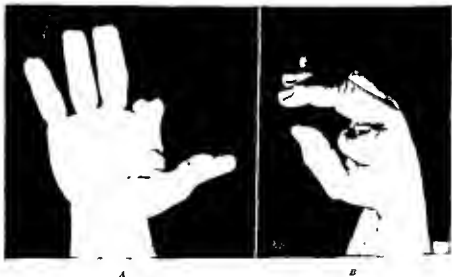


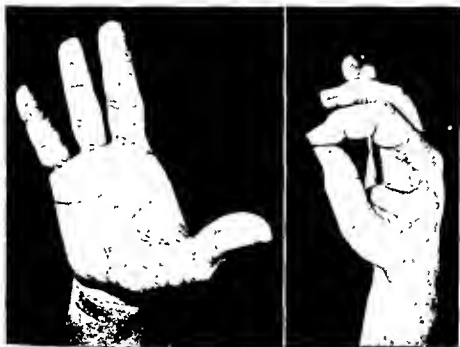
Fig. 3 (Case 2)—A, Volar view of the right hand. The index finger has been amputated through the middle third of the proximal phalanx, leaving a short stump of very little functional value.

B, Side view of same hand showing how the short index stump may interfere with the normal function of the remaining digits.

CASE 2—A 26-year-old first lieutenant, serving as a paratrooper in the infantry, was wounded in combat on Oct. 2, 1944, in Germany. He sustained multiple wounds, including a partial traumatic amputation of the right index finger. The wound of the right hand was treated by débridement and primary closure.

The officer was transferred to this general hospital on July 28, 1945, primarily for further treatment of an ununited fracture of the left femur. In addition, he requested consultation with the hand service because he felt that the right hand would be more serviceable if the stump of the index finger were amputated. This index finger stump was so short that it could not be opposed to the thumb and did not aid in grasping objects. He stated, "I am constantly bruising this stump when I use my right hand. This stump seems to draw bumps."

Examination of the right hand on June 8, 1946, revealed normal thumb, long, ring, and little fingers. The index finger was amputated through the middle third of the proximal phalanx, and the end of the stump was well covered with an adequate skin pad. Active range of motion in the second metacarpophalangeal joint was from 180 degrees extension to 100 degrees flexion.



A.

B.

Fig. 4 (Case 2).—A, Volar view of right hand, following index ray amputation and flexor tendon transfer at the wrist.

B, Side view of same hand, showing that the long finger now may assume the full duties of a normal index finger.

On June 10, 1946, amputation of the right index ray was performed, with a transfer of the flexor profundus tendon of the index finger into the flexor profundus tendon of the long finger at the wrist. The operative incisions healed by primary intention. Physical therapy, consisting of whirlpool baths and massage, was given for two weeks to aid in the restoration of normal motion in the fingers and thumb. The patient experienced some discomfort at the site of tendon transfer at the wrist when starting active motion in the fingers, but this subsided in a few days.

Although this patient is still hospitalized for further treatment of the fractured femur, he has already found that he is better able to use the right hand in walking on crutches or in performing other manual duties about the hospital.

**CASE 3.**—A 28-year old Army sergeant was taken prisoner at Bataan. While working as a prisoner of war in a coal mine, he sustained an injury to the left hand on June 6, 1945. The left index finger was crushed by a falling stone. A Japanese medical officer sutured the jagged laceration along the proximal phalanx of the finger without any previous cleansing or débridement of the wound. The finger became infected, and osteomyelitis developed in the proximal phalanx. A curettage of the draining wound was performed in September, 1945, and the index finger was placed in traction in a banjo splint when the soldier was evacuated.

to the United States. The wound healed by January, 1916, while the soldier was a patient in an Army general hospital. At that installation, the soldier requested that the index finger be amputated, but the opinion of the medical officers was that the finger should be saved. The soldier was transferred to another general hospital, where amputation of the index finger was again refused because the medical officers felt that this digit should be saved if at all possible.

The soldier was transferred to the hand service of this general hospital on May 24, 1916, for further evaluation and disposition. He still maintained that the injured finger was in his way and that the function of the hand would be improved a great deal by amputation of the index finger.



FIG. 5 (Case 3).—A, Volar view of left hand. Although the index finger has normal sensation, its joints and tendons have been irreparably damaged.

B, Side view of same hand, showing how the damaged index finger interferes with the function of the remaining normal digits.

Examination of the left hand revealed a normal thumb, long, ring, and little fingers. The index finger was shortened three-fourths of an inch. There was a scar on the radial side of the proximal phalanx, extending to the distal interphalangeal joint. Sensation was normal throughout the entire index finger. Range of motion in the second metacarpophalangeal joint was from 150 degrees extension to 110 degrees flexion, the proximal interphalangeal joint was fixed by bony ankylosis at 180 degrees; and the distal interphalangeal joint was also fixed at 150 degrees by a firm fibrous ankylosis. Roentgenograms revealed a healed comminuted fracture involving the shaft and head of the proximal phalanx and the base of the middle phalanx, with evidence of chronic osteomyelitis in the proximal phalanx and bony ankylosis of the proximal interphalangeal joint.

On June 2, 1916, amputation of the index ray was performed. The operative incision healed by primary intention. Physical therapy, consisting of whirlpool baths and massage,

was given for one week to aid in the restoration of normal motion in the fingers and thumb. The patient has expressed complete satisfaction with the increased dexterity and usefulness he now has in the left hand. He finds that the left long finger performs adequately the functions of a normal index finger.

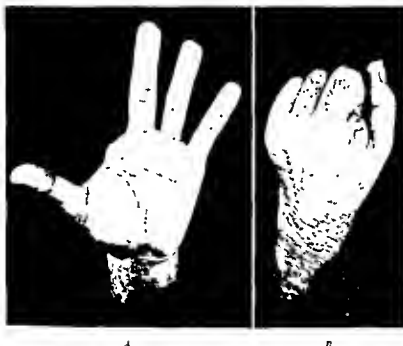


Fig 4—A, Volar view and B, side view of same hand as shown in Fig 3 after index ray amputation. The efficiency of this hand has been much improved by removal of the poorly functioning index finger and restoration of a wide smooth cleft between thumb and long finger.

#### DISCUSSION

During the past year, we have performed eighteen amputations of the index ray. In every case, the dexterity of the hand has been improved and the patient has expressed satisfaction with the end result. The cosmetic appearance of the hand has also been improved, but we have always considered this factor to be of only secondary importance. When recommending an index ray amputation, we have been primarily concerned in the restoration of an efficiently functioning hand; the fact that the cosmetic appearance of the hand is also improved becomes purely incidental.

In performing an index ray amputation, an incision is made about the base of the index finger and then extended longitudinally on the dorsum of the hand to the base of the second metacarpal. The second metacarpal is exposed subperiosteally and osteotomized just distal to its base. The base of this bone is not removed because it is desirable to preserve the insertion of the extensor carpi radialis longus tendon.<sup>1</sup> If possible, the tendon of the first dorsal interosseous muscle is isolated and inserted into the tendon of the second dorsal interosseous muscle. This tendon transfer does not materially increase the range



of abduction in the long finger, but it does increase the power of the long finger to resist pressure from the thumb. The digital nerves are carefully isolated, ligated, and buried to prevent the formation of painful neuromas. Through a small separate transverse incision at the wrist, the flexor tendons of the index finger may be withdrawn and transferred into the flexor tendons of the long finger. Obviously this tendon transfer should increase the flexion power of the long finger, but it is difficult, if not well-nigh impossible, to evaluate the clinical results of this procedure. In any event, we do not believe this flexor tendon transfer is an essential part of the operation.

It is true that amputation of the index ray does narrow the breadth of the palm, and this may not be too desirable in a patient who must perform heavy manual labor. It has been our experience, however, that the increased dexterity obtained by this operation more than compensates for the slight diminution in breadth of the palm. With an amputation through the second metacarpophalangeal joint, there would still be present a stump which would be constantly traumatized and which might interfere to some extent with an adequate pinching action between the thumb and long finger. In every case where index ray amputation was advised, the patient had had ample opportunity to use and work with the injured hand. Many of the patients had received "work furloughs" of sixty to ninety days, and some had been returned to military duty. All of the patients found, through experience, that the efficiency of their hands was markedly impaired by the injured or amputated index finger; all patients agreed that, following amputation of the index ray, the function of their hands was much improved. The majority of these patients performed manual labor for a livelihood.

#### SUMMARY

1. Amputation of the index ray is indicated in cases with an amputation of the index finger at any level proximal to the proximal interphalangeal joint, and in patients with an injured index finger not amenable to reconstructive surgery.

2. When only the index finger has been injured, and the remainder of the hand is normal, amputation of the index ray will restore almost normal function to the injured hand.

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## SURGICAL TREATMENT OF INGROWN TOENAIL

LIEUTENANT B. G. CLARKE AND LIEUTENANT K. A. DILLINGER,  
MEDICAL CORPS, U. S. N. R.

EXPERIENCE with 269 patients with ingrown toenails operated upon by Winograd's technique is summarized to augment the excellent studies already published including those of Dowd,<sup>1</sup> Kurtzahn,<sup>2</sup> Keyes,<sup>3</sup> and Winograd,<sup>4,5</sup> who presented statistical data on postoperative follow-up in their reports. The judgment of the surgeon will dictate the use of conservative treatment or selection of one of several types of operations. Each has been used successfully by its exponents in the past and present.

### HISTORICAL

Michaelis<sup>6</sup> reviewed work done before 1830, Emmert<sup>7</sup> abstracted contributions from that date until 1869, and Bartlett,<sup>8</sup> Keyes,<sup>3</sup> and Wilson<sup>9</sup> discussed more recent reports. A description of the anatomy of the toenail may be found in *A Textbook of Histology* by Maximow and Bloom.<sup>10</sup>

As early as 1830, Michaelis<sup>6</sup> pointed out the importance of cutting the toenails square with their corners exposed and of wearing well-fitted shoes to prevent ingrown toenail. This observation has been generally agreed upon since.

Among conservative methods of treatment, Heister<sup>11</sup> in 1763 elevated the corner of the ingrowing nail with a sound and maintained it in position with a piece of cotton thrust under the nail corner as a splint. The same method was described by Foote,<sup>12</sup> Deavor,<sup>13</sup> Graham,<sup>14</sup> Dodd,<sup>15</sup> Kendall,<sup>16</sup> Winograd,<sup>4</sup> O'Donoghue,<sup>17</sup> Christopher,<sup>18</sup> and others. The ingrowing nail corner may also be separated from the inflamed soft tissue with inelastic materials such as metal splints described as early as 1825 by Duden,<sup>19</sup> lately by Foote and Livingston,<sup>16</sup> Klages,<sup>18</sup> Marton,<sup>20</sup> and Lineh.<sup>21</sup> Celluloid-soaked gauze was used by Mickel.<sup>22</sup>

Dodd<sup>15</sup> gave instructions for another conservative technique which he has used successfully: the center of the nail is shaved with knife, glass, or emery board and a V-shaped notch is clipped in its end. This method, employed by LaFaye<sup>23</sup> in 1739, has met with the approval of many since.

Albucasis<sup>24</sup> treated ingrown nail in the eleventh century by excision and cautery of the exuberant granulation tissue. During the nineteenth, caustics and escharotics were widely used. Among contemporaries, Vernon<sup>25</sup> has successfully employed electrosurgery for the same purpose although his report does not specify the average time required for healing.

Surgical excision of the granulating soft tissue was practiced by Ambroise Paré<sup>26</sup> four hundred years ago. Emmert<sup>7</sup> and Cotting<sup>27</sup> devised operations for more extensive excision of the granulating tissue together with a segment of nor-

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mal tissue from the side of the toe. As the defect healed by cicatrization the soft tissues and skin were withdrawn from the nail corner. Healing by this method, according to Cotting,<sup>21</sup> required four weeks. Ney<sup>22</sup> in 1923 described the extensive resection of soft tissue from the side of the toe followed by plastic skin closure of the defect, which required from two to three weeks for complete healing.

Retraction of the irritated soft parts from the margin of the nail is the basis also of an operation described in 1893 by Howard,<sup>24</sup> who excised an elliptical, wedge-shaped segment of skin and soft tissue from the uninfected area at the end of the toe and sutured the defect to withdraw the inflamed part from the ingrowing nail edge. Bartlett<sup>8</sup> successfully employed a less extensive incision, removing a wedge of tissue from the side of the toe to achieve the same result. These techniques require incision only through uninfected areas and favor primary healing and short convalescence.

Inflamed tissue is removed from the nail in the foregoing types of operation. In currently more widely practiced techniques the ingrowing nail margin is removed. Fabricius,<sup>4</sup> seventeenth century Italian anatomist and surgeon, the pupil of Fallopius and teacher of Harvey, excised and avulsed the ingrowing margin of the toenail. He was followed by Heister and Michaelis.<sup>6</sup> Agard,<sup>25</sup> Anger,<sup>26</sup> and Dowd<sup>1</sup> modified this maneuver to include excision not only of the ingrowing nail margin but of the lateral skin fold, the granulating soft tissue, and the nail-bearing matrix as well. In ten of Dowd's twenty-three cases, healing was by first intention. In 1899 Foote<sup>11</sup> published a less radical variation of this technique which has been discussed by Fabry,<sup>27</sup> O'Donoghue,<sup>14</sup> Christopher,<sup>28</sup> and others. This is called the standard or von Bergmann operation by Keyes.<sup>29</sup> A wedge of tissue is excised down to the periosteum of the terminal phalanx to include a strip of nail about one-fourth inch (0.5 cm.) wide, the underlying nail bed and matrix, and the adjacent lateral skin fold and ulcer. The matrix is curetted and each end of the wound may be approximated by stitches. Kurtzahn<sup>7</sup> reported no recurrence in twenty-five patients observed for one and one-half years postoperatively. In sixty cases studied by Keyes<sup>2</sup> in which the same technique was used by a group of surgeons, there were three recurrences. Sixteen days were the average required for healing in this series; in three patients healing was by first intention. In a basically similar procedure, Thurlow<sup>31</sup> and Bennett<sup>32</sup> developed methods of plastic closure which are described in their articles. Although Bennett does not give figures on recurrence, his patients were walking in three days and ready for military duty in seven.

The most radical procedure for cure of ingrowing nail is removal of the entire nail. It is generally agreed that without curettage of the matrix, recurrence is frequent. Dupuytren<sup>6</sup> in 1826, however, excised and avulsed the nail and destroyed the matrix. Deavor<sup>12</sup> and Scougall<sup>13</sup> described the same technique although their report does not contain statistics; among Keyes<sup>2</sup> group, three patients were operated upon in this fashion with no recurrences and an average healing time of twenty-three days. Removal of nail and matrix with plastic closure of the defect by mobilization of skin flaps proximal and distal to the

site of the nail has been done by Dolan,<sup>24</sup> Kendall,<sup>15</sup> Eichelbaum,<sup>25</sup> Nuttall,<sup>24</sup> and Wilson,<sup>9</sup> who described their methods. In Keyes'<sup>2</sup> series, four cases were done by a plastic method, with one recurrence.

Winograd's technique, outlined in his articles<sup>4, 5</sup> and in Christopher's *Minor Surgery*,<sup>11</sup> is a refinement of Fabricius' made possible by use of an anesthetic. The nail-forming matrix is exposed by a small incision in the eponychium, and after removal of a one-eighth to one-quarter inch (0.3-0.6 cm.) strip of ingrowing nail, the matrix and nail bed are curetted leaving the soft tissues otherwise intact. Winograd<sup>5</sup> did a follow-up study on twenty cases for eighteen months, in which there were three recurrences. In Keyes'<sup>2</sup> series of thirty-four cases, there were four recurrences. Among twenty-nine of our Naval cases followed closely, nine recurrences were noted, two with symptoms. Among a group of 240 Marines operated upon, among whom systematic follow-up was not made, only one recurrence was known. Primary healing occurred in our entire series of 269 cases which may be attributable to favorable age group of patients, the simplicity of the procedure, and uniform preoperative preparation consisting of surgical scrub of foot with hand brush, soap, and water. Foote<sup>14</sup> in 1899 emphasized the importance of scrubbing and disinfecting the toe. Graham<sup>12</sup> used a technique similar to that of Winograd, dissecting rather than curetting the matrix. He did not give figures on recurrence.

#### REPORT OF CASES

Two groups of cases are included in this study. Twenty-nine operations were performed aboard a Naval vessel. These represented an annual incidence of 29 per 1,000 men. Two hundred forty operations were performed upon men of an expeditionary unit of Marine infantry, representing an annual incidence of 113 per 1,000 men. Each operator used Winograd's technique without modification, using digital nerve block with procaine hydrochloride.

Conditions aboard ship favored preservation of records and extended follow-up. The twenty-nine operations were done on twenty sailors whose average age was 25 years, between 18 and 30. No case was included in the study on which follow-up was for less than three months, which proved to be enough time to detect recurrence. The average period of observation was eight months, the longest, eighteen. The operation was performed only when pain was caused by an ingrown toenail, with or without marked soft tissue hypertrophy and granulation. In five men paronychia and abscess formation had occurred previously. Two men had operations elsewhere for ingrown toenail with recurrence. In all cases, the great toe was affected, in six the right only, in seven the left only, in seven, both big toes. Twenty-one operations were on the medial nail margin, four on the lateral margin, and two on both sides of the toe, making twenty-nine operations in all. When infection was present, several days' treatment were directed toward its amelioration or localization by conservative methods.

In each of these cases the patient scrubbed his foot before operation using a surgeon's hand brush, soap, and water in the fashion of a surgeon's hand scrub for ten minutes, under the supervision of the surgical corpsman. Skin was

prepared with tincture of merthiolate, 1:1000, and aseptic technique was employed. In every case primary healing occurred without infection. Post-operative discomfort was negligible; mild sedatives or analgesics were used occasionally. Petrolatum gauze and a snug bulky dressing were applied at operation and left for six to twenty-four hours during which the man remained in his bunk with the foot elevated. He was then allowed up with dry sterile dressing which became unnecessary after the fourth to seventh day. Men returned to duty, depending upon the nature of their work, in two to five days. In nine cases, or 31 per cent of the group, small regrowths of nail appeared from the curetted nail bed, two of which eventually caused pain.

Among the Marines, follow-up was more difficult. It was the surgeon's impression that the relatively high incidence of the disorder in this group of infantrymen was accounted for by heavy shoes and tropical expeditionary conditions. When necessary, conservative preoperative treatment was administered to reduce infection in the involved toe. Each patient was required to scrub his foot for five minutes with hand brush, soap, and water before operation under supervision of a hospital corpsman. Skin was prepared with tincture of merthiolate, 1:1000, and modified sterile technique, without gloves, was observed. Winograd's operation was performed, in a few cases modified to the extent that when large mass of exuberant granulation was present this was excised. Sterile crystalline sulfanilamide and petrolatum gauze were applied. The patient remained on a cot for twenty-four hours with the foot elevated, when the dressing was replaced by dry sterile gauze and he was allowed up. Healing was by first intention in all cases. Men were ready for full military duty, without dressings, in three to five days. Because of high casualty rates and combat conditions, accurate records and follow-ups were not kept. In only one instance, however, did a case of recurrence come to the surgeon's attention.

#### COMMENT

Survey of existing publications indicates that prevention of ingrown toenail depends on trimming the ends of the toenails square and the use of well-fitted shoes. Acceptable methods of conservative treatment include elevation of the ingrowing nail corner and splinting with cotton or other material; or shaving the center of the nail and notching its free end. Electrosurgery as well as several techniques for excision of exuberant granulation tissue have been employed, although healing may require some time in certain of these techniques. The nail and its matrix may be removed completely and allowed to heal by granulation, or the defect may be closed by mobilization of skin flaps and plastic repair. Another technique is the removal of a wedge-shaped block of tissue including the ingrown strip of nail, adjacent skin fold, and granulation tissue, with curettage of the nail matrix and bed. Of eighty-three patients treated thus, cases in which figures are available, three had recurrences. Winograd's technique consists of removal of a nail strip including the ingrowing part and curettage of the nail-forming matrix and nail bed through a small eponychial incision leaving the soft tissues otherwise intact.

Among the cases in which follow-up was carried out by Winograd and Keyes,<sup>3</sup> seven of fifty-four included recurrences. In the present study, primary healing occurred in all of 269 cases, which may be attributable to favorable age of the patients, the simplicity of the procedure, the use of aseptic technique, and uniform preoperative preparation of the foot by surgical scrub with hand brush, soap, and water. Among closely followed Navy personnel there were nine recurrences in twenty-nine cases, two with symptoms. Among 240 Marine infantry men who were not followed, only one recurrence came to the surgeon's attention.

## SUMMARY

1. Results of operation for ingrown toenail by Winograd's technique in 269 cases are considered, and other conservative and operative methods of treatment are discussed.

2. Primary healing occurred without infection in all cases, which may be attributable to favorable age of patients, simplicity of procedure, use of aseptic technique, and uniform preoperative preparation of the foot by surgical scrub with hand brush, soap, and water.

3. In twenty-nine closely followed cases, there were nine recurrences, two with symptoms.

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